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1844	6*	*for* " acid " *read* " alkaline."
1846	31	*for* " dissolved " *read* " suspended."

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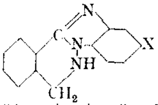
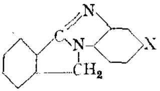
95	formula (IX)	*for*  *read* 
521	8	*for* " isomeric oximes " *read* " isomeric 3-halogenonitrosophenols.

* From bottom.

JOURNAL

OF

THE CHEMICAL SOCIETY.

1. *The Acid Fluorides of the Alkali Metals. Part I. The Acid Fluorides of Rubidium.*

By E. B. R. PRIDEAUX and K. R. WEBB.

OUR knowledge of the acid fluorides of rubidium was principally due to Eggeling and Meyer (*Z. anorg. Chem.*, 1905, **46**, 174), who described the preparation of the bifluoride, RbF,HF, and of a mixed salt of RbF,2HF (containing also some RbF,3HF) and gave an account of the apparent stability and solubility of these substances. Since some of their statements, especially those referring to the insolubility of RbF,2HF and its apparent great stability towards heat, were rather improbable, it was decided to examine the matter further and to prepare the bifluoride, and possibly higher fluorides, in a state of greater purity.

Considerable progress had been made when Meyer and Taube (*ibid.*, 1936, **227**, 337) reported that the supposed insoluble acid fluoride of rubidium is really the silicofluoride Rb_2SiF_6 (see also Finbak and Hassel, *ibid.*, 1936, **226**, 175). They proved that an acid fluoride can be prepared from rubidium carbonate and aqueous 40% hydrogen fluoride. Any insoluble silicofluoride at first precipitated is removed, and the filtrate evaporated until it sets to a solid mass on cooling. The residue, on being heated at 150° in a drying oven, lost only 4·62% of its weight. The solid, when ground, and kept over concentrated sulphuric acid in a glass desiccator for several days, gave, on analysis: Rb, 59·2, 59·3; HF, 26·61, 26·94 (Calc. for RbF,2HF : Rb, 59·16; HF, 27·67%). We have confirmed and extended these results.

Higher Acid Fluorides of Potassium and its Congeners.—Prior to Moissan's work on the isolation of fluorine, potassium bifluoride (Frémy's salt) was the only known acid fluoride of potassium. Moissan (*Compt. rend.*, 1888, **106**, 548) obtained KF,3HF from the bifluoride either by cooling its solution in anhydrous hydrogen fluoride to $-23°$, or by warming it with the calculated quantity of hydrogen fluoride in an oil-bath at 85°. The product, which set to a hard mass at 68°, was deliquescent and evolved hydrogen fluoride in a moist atmosphere, but was stable in dry air. The pressure of hydrogen fluoride at 100° was found to be 30—50 mm. by Wartenberg and Klinkott (*Z. anorg. Chem.*, 1930, **193**, 409). On electrolysis of this fused salt, fluorine was obtained by these workers, and also by Lebeau and Damiens (*Compt. rend.*, 1925, **181**, 917). By suitably altering the proportion of hydrogen fluoride in his second method, Moissan prepared KF,2HF, for which Lebeau gives m. p. 70°, and Cady (*J. Amer. Chem. Soc.*, 1934, **56**, 1431) m. p. 71·7°. The latter investigator, from measurements of vapour pressures and freezing points of the system KF–HF, reported two further acid fluorides, KF,4HF and 2KF,5HF.

For the preparation of fluorine by the electrolysis of fused acid fluorides, those of potassium had generally been used, but when cæsium became more readily available, Mathers and Stroup (*Trans. Amer. Electrochem. Soc.*, 1934, **66**, 113) utilised its acid fluorides for this purpose because they were more readily fusible. From the carbonate and the aqueous acid, both CsF,1½HF, m. p. 30°, and a product of approximate composition CsF,2HF, m. p. 19°, were obtained. CsF,HF had previously been described by Chabrie (*Compt. rend.*, 1901, **132**, 680).

Experimental.

Preparation of KF,2HF.—It would be very convenient if the more fusible higher fluorides of potassium could be prepared without the use of anhydrous hydrogen fluoride, since their high content of hydrogen fluoride and ready fusibility make them valuable for studying the action of hydrogen fluoride upon various materials at moderate temperatures, as Moissan pointed out. In spite of repeated trials, we have been unable to prepare any fluoride higher than KF,HF by evaporation of aqueous solutions by heat. More success attended evaporation over sulphuric acid in a desiccator (cf. Prideaux and Millot, J., **1929**, 2703), whereby, from KF,HF and 40% hydrogen fluoride, crystals were obtained, which contained HF, 38·39 (mean of two results) (Calc. for KF,2HF : HF, 40·82%); m. p. *ca.* 80°. This product contained, however, a small quantity of silicofluoride derived from the glass of the desiccator, which cannot be completely protected by any coating—in this instance, wax (ceresin) was used, but was not entirely satisfactory. Further examination of this compound is therefore postponed until the work can be repeated in apparatus free from glass.

Method of Analysis.—Since only small amounts of the rubidium compounds (see below) were available, it was necessary to devise a method of analysis which would allow the rubidium to be recovered from all residues in a convenient form, free from alkali metals. Therefore, the free acid was neutralised with excess of ammonia, and the excess determined by back-titration with hydrochloric acid, bromothymol-blue being used as indicator. A good end-point was obtained at p_H about 7·5, and control experiments with dilute hydrogen fluoride solutions showed that the results by this method agreed within the limits of experimental error in titration (0·3%) with those given by direct titration with carbonate-free sodium hydroxide and phenolphthalein as indicator.

Acid Rubidium Fluorides.—Materials. The source of rubidium was the carbonate, supplied by the Burbach-Kaliwerk A.G. and guaranteed chemically and spectroscopically pure. In view of the known deliquescence of potassium carbonate, the loss on ignition of a specimen of the rubidium carbonate was found : it was 0·75%.

The dilute hydrofluoric acid used was 36—40% A.R. quality, supplied in ceresin bottles. The anhydrous hydrogen fluoride was prepared by heating sodium bifluoride of good quality free from silicofluoride. The salt was previously dried by heating at 100—110° for some hours, and cooling in a desiccator. The distillation of the bifluoride was conducted in the copper apparatus previously described (Prideaux and Millott, J., **1926**, 167); external joints were luted with glycerol–litharge cement, and addition of a little lead fluoride seemed to improve its properties at higher temperatures. Platinum vessels were used exclusively for the preparation and manipulation of the acid fluorides.

Rubidium bifluoride, RbF,HF. This was easily prepared by dissolving rubidium carbonate in a slight excess of the 36% acid. A clear solution was obtained, showing the absence of silicofluoride, and was evaporated to a small bulk. On cooling, it set to a hard white mass (Found : HF, 16·54; whence Rb, 68·3.* Calc.: HF, 16·07; Rb, 68·6%), the weight of which agreed closely with the theoretical. The salt was therefore purer than that prepared by Eggeling and Meyer (*loc. cit.*), which had Rb, 66·7%. They attributed the discrepancy to the deliquescent nature of the bifluoride. This would, however, be in strong contrast to the property of the potassium analogue, which at most is only slightly hygroscopic. We have found, in fact, that exposure to ordinary atmospheric conditions for an hour leads to no gain in weight, and the gain even from a moist atmosphere in a similar time was less than 1%. The saturation pressure of hydrogen fluoride over this compound is low, probably lower than that of potassium bifluoride, but, in agreement with Meyer and Taube, we find that the acid is completely volatilised below red heat, with production of neutral rubidium fluoride. The m. p. of the substance is undoubtedly lower than that of the potassium compound : by heating a little of the substance in a platinum crucible in an oil-bath, it was found to be about 207°. A more accurate determination was made by heating a larger quantity in a platinum crucible to 220° in an oil-bath and allowing the liquid to cool whilst being stirred with a thermometer protected by a silver sheath (not appreciably attacked by the melt) made for the purpose : the value thus found by several trials was 204—205°.

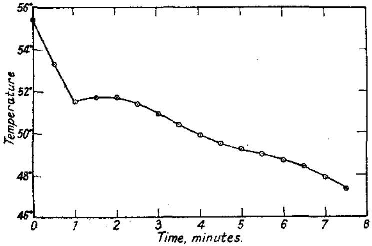
RbF,2HF. This compound was prepared in the waxed desiccator (see above) by evaporation of a solution of the bifluoride in 36—40% acid with greater ease and in a purer condition than the potassium compound. It is not necessary to segregate the solid material which separates round the edges of the dish, as in the case of potassium : the whole mass is allowed to become solid and dry, the compound, surrounded by an atmosphere rich in hydrogen fluoride, resulting

* RbF is found by difference.

(Found: HF, 26·76. Calc.: HF, 27·68%. Meyer and Taube found 26·78%). In agreement with Meyer and Taube, we attribute the low result to the presence of a small quantity of silicofluoride. Excessive corrosion of the desiccator under the ceresin is also evident in some cases in the preparation of salts of this type. In the dry state, as a solidified melt, RbF,2HF has only a slight pressure of hydrogen fluoride, and even in the fused state above 60° the loss of the fluoride is very slow; at about 100—110°, it is appreciable, especially after repeated fusions. The substance is deliquescent, and after a little moisture has been absorbed, the loss of hydrogen fluoride on heating appears to be greater. Meyer and Taube report that it is converted into RbF,HF at 150—190° after some hours.

Those authors did not determine the m. p., but an approximate determination by the method already described showed it to be slightly above 50°.

An apparatus for taking cooling curves of such substances was devised. The salt was contained in a small platinum crucible, into which were inserted a silver wire stirrer and a nickel-plated tube which contained a thermometer graduated in 0·1°. The crucible was surrounded by a thin-walled metal pot, which was kept at a suitable constant temperature by immersion in a large vessel of water, covered with a layer of oil. The crucible stood in the metal pot upon an ebonite pad and therefore was not in direct thermal contact with the metal itself.



Cooling curve of RbF,2HF.

The salt was melted by placing the crucible in an oil-bath. The crucible was then inserted in the metal pot, and the temperature read every ½ minute. In early experiments, without stirring, the degree of supercooling was very great, the temperature rising from 46° to 50° as the material solidified. By vigorous stirring it was greatly reduced, as shown in the figure. The closest estimate for the m. p. is 51·6—51·7°. A second slight inflection in the graph, observed at 49°, may be due to transition into another crystalline form or to the separation of a lower fluoride from the melt.

The m. p.'s of various acid fluorides of the alkali metals are given in the table.

Melting Points of Acid Fluorides.

KF,HF	KF,2HF	KF,3HF	RbF,HF	RbF,2HF	RbF,3HF
217° [1]	71·5° [2]	65° [3]	204—205° [4]	51·7° [4]	>0° [4]
	CsF,HF	CsF,1½HF	CsF,3HF	CsF,1½—2HF	
	142° [5]	30° [5]	—	19°	

[1] Dennis, Veeder, and Rochow (*J. Amer. Chem. Soc.*, 1931, **53**, 3263). [2] Cady (*loc. cit.*). [3] Moissan (*loc. cit.*). [4] Present paper. [5] Mathers and Stroup (*loc. cit.*).

RbF,3HF. The foregoing experiments have shown that very concentrated or anhydrous hydrogen fluoride would be required in the preparation of acid fluorides higher than RbF,2HF, and by using the latter, we have isolated a new *substance* which appears to be RbF,3HF. Anhydrous hydrogen fluoride, prepared in the manner and apparatus already described, was kept cooled in a covered platinum crucible, and about 2 g. of RbF,HF were added, which dissolved with a hissing sound. Some brownish flocculent precipitate, apparently due to organic matter, was filtered off in a platinum Gooch crucible fitted with platinum-gauze pads, and the clear colourless liquid was cooled in a solid carbon dioxide–ether mixture, in which it solidified to a pasty mass, which melted again below 0°. On addition of further quantities of the two

reactants and cooling as before, a fairly hard solid was obtained, which on warming to about 20° gave a mush of transparent crystals. A portion was filtered off and pressed, and about 0·1 g. was rapidly weighed and analysed (Found : HF, 36·98. RbF,3HF requires HF, 36·47%). After standing for a week, the liquid still contained clear colourless crystals, which obviously had the same refractive index as the surrounding liquid. The mother-liquor then contained HF, 37·73%, so it seems that the crystals, being in contact with a liquid of nearly the same composition, had nearly the maximum freezing point, *i.e.*, nearly the m. p. of the pure compound. An attempt is being made to determine more fully the conditions of existence and the physical constants of this highest fluoride. It is probably incapable of existence in the presence of even a small amount of water, since the above solution, which gradually attracted some moisture during manipulation, gave, on careful evaporation by heat, only RbF,2HF (Found : HF, 28·58. Calc. : HF, 27·68%) with a slight excess of hydrogen fluoride. Undoubtedly, RbF,2HF could be prepared in a state of purity by maintaining the higher fluoride in a fused state for some time, with stirring to expel the excess hydrogen fluoride.

CONCLUSIONS.

(1) Under suitable conditions, an acid fluoride of potassium approximating in composition to KF,2HF can be obtained from dilute (36—40%) hydrofluoric acid.

(2) The acid fluoride RbF,HF can readily be prepared from dilute hydrofluoric acid and pure rubidium carbonate. It has m. p. 204—205° and is not deliquescent.

(3) The acid fluoride RbF,2HF can be prepared in an analogous manner to that of potassium, but in a purer state, by using the special method described; its m. p. is 51·7°.

(4) From preliminary experiments, the existence of a higher hydrofluoride of rubidium, RbF,3HF, is indicated, but this can only be obtained by using anhydrous hydrogen fluoride.

(5) The acid fluorides of rubidium resemble those of potassium in their general properties and heat stability.

Further work is in progress on the higher acid fluorides of rubidium.

We thank the Chemical Society for a grant for the purchase of rubidium carbonate.

UNIVERSITY COLLEGE, NOTTINGHAM. [*Received, October 23rd, 1936.*]

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2. *Combination of Fatty Acids with Nitrogen Bases. Part II. Piperidine and Lower Fatty Acids: Conductivities and Viscosities of Liquid Anhydrous Salts.*

By E. B. R. PRIDEAUX and R. N. COLEMAN.

IN Part I (J., 1936, 1346) the existence of a definite conductivity was adduced as evidence that the piperidine salts of the lower fatty acids contain a certain proportion of free ions. This work will now be described in more detail.

Conductivities of the Salts.—The Kohlrausch method is not well suited for the determination of the conductivity of oily liquids on account of uncertainties in the nature of products of polarisation at platinised electrodes and the practical difficulty of obtaining a good telephone minimum in liquids of such low conductivity. We therefore used Gram and Cullen's method (*J. Biol. Chem.*, **1923**, **57**, 477), in which the fall of potential across a known resistance (60,000 ohms) is compared with the fall across the same resistance with the cell in series; the direct current of the mains was used. If E_1 and E_2 are the respective falls of potential observed across the resistance, the resistance, R, of the cell is given by $R = 60{,}000(E_1 - E_2)/E_2$. The method has been used by one of us in measuring the conductivities of protein solutions (*Trans. Faraday Soc.*, **1935**, **31**, 349), and has been checked by the Kohlrausch measurements. The salts were prepared by mixing weighed stoicheiometrical quantities of the constituents, special precautions being taken to prevent access of moisture. They were transferred to the conductivity cell by a special device, which likewise avoided contact with air. (The cell was stoppered, sealed with collodion, and placed in a ther-

mostat at 25°, regulated to within 0·02°.) These precautions were necessary, since some earlier results with specimens dried by anhydrous sodium sulphate were found to be in error on account of the extremely hygroscopic nature of the salts, which gave values for conductivities higher than those finally observed. We consider, however, that values obtained with these precautions are a close approximation to the true conductivities (κ) of the salts. From the molar volumes previously determined, the molar conductivities (Λ) were calculated. The results are summarised in Table I. It was possible to read the voltmeter to within 0·2 volt (the p.d. being of the order of 200 volts); so that a value for the conductivities could be obtained correct to three significant figures.

TABLE I.

Salt.	$\kappa \times 10^4$.	Λ.	Salt.	$\kappa \times 10^4$.	Λ.
Propionate	5·47	0·0851	Hexoate	3·17	0·0657
Butyrate	4·54	0·0784	Heptoate	2·80	0·0627
*iso*Valerate	2·03	0·0388	Octoate	2·15	0·0520

With the exception of the salt of the branched-chain acid, the *iso*valerate, these salts thus show a progressive diminution of conductivity with increase of molecular weight.

Variation of the Conductivity with Temperature.—The heptoate was chosen for this experiment. The ends of a small U-tube were joined by sealing on a Y-piece. Through the open end the apparatus was successively washed with water, ether, and dry ether, and dried by a current of warm dry air. The salt was introduced with a minimum access of air, and the vessel was then partly evacuated through drying tubes and sealed. The sealed-in platinum electrodes were protected by external tubes bent upwards, and were connected by mercury, with copper-wire leads passing down these tubes. The conductivity cell could thus be completely immersed in water. Conductivities were taken at intervals of about 5° from 15° to 60°, by adjusting the thermoregulator of the thermostat, and were quite steady and reproducible. They are given in Table II, together with molar conductivities, calculated from previous determinations of the variation of density with temperature.

TABLE II.

Temp.	15·4°	20·8°	25·0°	30·1°	35·2°	39·7°	44·8°	50·0°	54·6°	59·9°
$\kappa \times 10^4$	1·63	2·20	2·80	3·50	4·49	5·32	6·52	7·77	9·08	10·54
Λ	0·036	0·049	0·063	0·079	$0{\cdot}101_5$	$0{\cdot}120_5$	0·148	$0{\cdot}177_5$	0·208	0·240
$\Lambda\eta$	—	0·0930	0·0881	0·0816	0·0766	0·0700	0·0654	0·0614	0·0578	0·0513

The variation of specific conductivity with temperature follows a smooth curve of the usual form. The temperature coefficients, α, calculated by the formula $\alpha = (d\kappa/dt)/\kappa$, are 0·049 at 25°, and 0·028 at 60°. The variation of molar conductivity with temperature, t, agrees with the equation $\Lambda = 5{\cdot}375 \times 10^{-5}t^2 + 5{\cdot}25 \times 10^{-4}t + 0{\cdot}0152$.

Comparison with Fused Salts.—Conductivities of typical ionised salts are as a rule much higher than those of the present type; *e. g.*, for KCl (776°), $\kappa = 2{\cdot}240$; for $NaNO_3$ (310°), $\kappa = 0{\cdot}977$; for NaCl (850°), $\kappa = 3{\cdot}50$. A closer comparison can be made with the alkylammonium picrates studied by Walden, Ulich, and Birr (*Z. physikal. Chem.*, 1928, **131**, 1), since these have lower m. p.'s (*ca.* 150°); as a result of the determination of the conductivities in the fused state and in non-dissociating solvents, such as chloroform and dichloromethane, it was concluded that the tetra-substituted compounds were almost completely dissociated in the fused state, whereas the less highly substituted compounds were largely undissociated. Typical values are:

Salt	$(C_3H_7)NH_3Pic$	$(C_3H_7)_4NPic$	$C_5H_{11}N,C_2H_5{\cdot}CO_2H$
$\kappa \times 10^4$	61·06	139·8	5·47
Λ	1·311	5·188	0·0851

It appears that piperidinium propionate at 25° has a rather lower conductivity than the lower-substituted alkylammonium picrates at 150°, but if the difference of temperatures and consequent difference of ionic mobilities are taken into account, it may well be that the conductivities are of the same order. If, therefore, the theory that conductivities of the

order shown by the lower-substituted picrates indicate a partial dissociation be extended to the salts under consideration, it will be concluded that they, too, are largely undissociated in the liquid state. The term "undissociated" is here taken in the sense of Bjerrum's more recent definition. Thus, in the equation $C_5H_{11}N,C_3H_7{\cdot}CO_2H \rightleftharpoons C_5H_{11}NH^+ + C_3H_7{\cdot}CO_2^-$, the symbol on the left denotes, not undissociated molecules, but ions associated in pairs. According to Bjerrum, it is characteristic of strong electrolytes that their ions do not undergo any significant changes of properties when they are combined : the ions can approach closely without appreciable deformation. On the other hand, we may assume that the present compounds appear to be weak electrolytes, the undissociated molecules consisting of pairs of ions, linked by a polar binding, having undergone at the same time strong deformation. The actual existence of a covalent link between the acid and piperidine, which is required by truly undissociated compounds, would appear to be impossible, since nitrogen can hardly exceed its octet of electrons, for, according to Sidgwick's theory of valency, this can only take place with elements of the second short period and onward.

In support of the present views as to the constitution of these salts there is also the fact that ions of large volume are more deformable than those of small volume. The connection between molecular volumes and the structure of fused salts has been studied by Klemm (*Z. anorg. Chem.*, 1926, **152**, 295), who showed that molten molecules have a relatively high, and ions a low, molar volume. Walden showed that the picrates of the tetrasubstituted ammonium bases had low molar volumes. In Part I (*loc. cit.*) it was shown that those of the piperidine salts of the fatty acids are only slightly less (approximately 15 units) than the sums of the values of the constituents; and the molar volumes are therefore large compared with those of ordinary salts. According to Klemm's hypothesis, the salts will be largely molecular, *i.e.*, the ions will be much deformed. This is also supported by the fact that the conductivities of the higher members become progressively lower, indicating that the salts are becoming more molecular in character; at the same time, the deviation of the observed molar volume from the additive relation becomes less, indicating a relatively larger molar volume.

The temperature coefficients of conductivity also throw light upon the constitution. According to Biltz (*Z. anorg. Chem.*, 1924, **133**, 306), the temperature coefficients of strong electrolytes are lower than those of weak electrolytes. For sodium chloride, α (see above) is 0·0009; for aluminium chloride, a weak fused electrolyte, α is 0·02; and for piperidinium heptoate, it is about 0·04 (mean value). In this respect also, the piperidinium salt belongs to the class of weak electrolytes.

Variation of Conductivity with Composition.—The electrical conductivities of the binary liquid system, acid–base, have been investigated by several workers. Aniline–acetic acid and pyridine–acetic acid were studied by Trifonow and Tscherbow (*Ann. Inst. Anal. Physico-Chim.*, 1926, **3**, 459), and aniline–phenol by Howell and Robinson (J., 1933, 1032). If the results were plotted as mols.% against specific conductivities, curves were obtained convex to the concentration axis, and falling to the zero conductivities of the pure components at each end. Aniline–acetic acid mixtures show a maximum at 17 mols. % of aniline, and pyridine–acetic acid a maximum at 80 mols.% of the acid. It was concluded that maxima correspond to the formation of dissociated compounds, but that they are always displaced to the side of the component with the lower molecular weight and viscosity. These conductivities however, changed with time and were not absolute values. In the system phenol–aniline, studied by Howell and Robinson, conductivity begins to rise sharply at about 1 phenol : 2 aniline, attributed to the formation of a compound of this composition. The maximum occurs at 83 mols.% of phenol, *i.e.*, aniline phenoxide in excess of phenol. The conductivity–composition curves of allylthiocarbimide with piperidine, *o*-toluidine, and aniline show two maxima with a sharp minimum at 50 mols.% (Trifonow *et al.*, *Bull. Inst. rec. biol. Perm*, 1931, **7**, 343).

Conductivities of piperidine and hexoic acid in various proportions were determined by the technique already described. The results are included in Table III and shown graphically in Fig. 1. The curve shows two maxima, one on the piperidine and one on the acid side, at 35 and 74 mols.% of acid respectively. These are rather more marked when molar, instead of specific, conductivities are plotted, and occur then at 33 and 78 mols.% of acid

respectively. Molar conductivities are calculated on the basis of g.-mols. of salt present per litre of the mixture.

TABLE III.

Acid, mols. %.	$\kappa \times 10^4$.	Λ.	$\Lambda\eta$.	Acid, mols. %.	$\kappa \times 10^4$.	Λ.	$\Lambda\eta$.
13·4	0·16	0·0118	0·0007	62·0	3·39	0·0964	0·1133
22·5	1·33	0·0589	0·0054	68·7	3·66	0·1296	0·0855
31·8	4·40	0·1391	0·0267	76·2	3·75	0·1796	0·0575
42·3	4·13	0·0994	0·0698	78·8	3·45	0·1869	0·0464
50·0	3·17	0·0657	0·1042	83·7	1·63	0·1170	0·0205
57·2	3·17	0·0788	0·1294				

The present case would appear to be a good example of Trifonow and Tscherbow's rule, the existence of two maxima (not found in mixtures of the acid–base type previously reported) confirming the chemical individuality of the salt, the maximum conductivity due to which is shifted to the side of each component of lower molecular weight and viscosity, *i.e.*, the free base and the acid. It was suspected that the intermediate minimum at the salt composition was due chiefly, if not wholly, to viscosity effects. It was therefore decided to determine viscosities, η, in order to supply data for the product $\Lambda\eta$, and also to extend the comparison of these systems to yet another physical property.

FIG. 1.

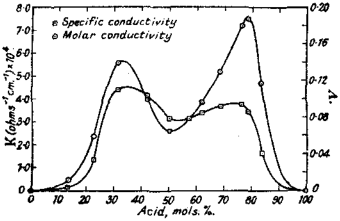
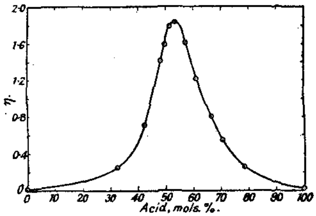


FIG. 2.



Variation of Viscosity with Composition.—It is obvious that the viscosities of the salts are much higher than those of either constituent, following a general law that, in the same system of acid–base, maximum values of η are connected with maxima of electrolytic dissociation. It is generally agreed that a better comparison of mobilities is obtained when the Λ values are corrected for viscosity by using the product $\Lambda\eta$.

The Ostwald–Poiseuille viscometer was calibrated with a 60% sucrose solution, having a time of outflow of 302 seconds at 25°. This solution has η 0·4402 (" International Critical Tables "), and d 1·2847. Every precaution was taken to exclude moisture both in preparing the various mixtures and during the actual experiment, as it was found that a small trace of moisture had a large effect in lowering the viscosity. In mixtures on the acid side of the curve, the limbs of the apparatus were connected with tubes containing loosely packed calcium chloride; for those on the piperidine side this was replaced by anhydrous sodium sulphate. Density values were interpolated from previous results. The variation of η with mols.% of acid is given below, and represented graphically by Fig. 2.

Acid, mols. %	0·0	32·3	42·5	48·6	50·0	51·7	53·7
η	0·022	0·204	0·711	1·414	1·586	1·785	1·833
Acid, mols. %	57·6	61·4	66·7	70·5	78·3	100·0	
η	1·618	1·221	0·808	0·551	0·262	0·028	

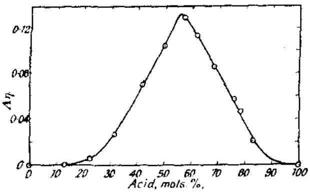
The values for the pure acid and base are taken from Landolt–Börnstein's " Physico-Chemical Tables."

The pronounced maximum in the viscosity curve is evidently connected with salt form-

ation, although it does not occur exactly at the equivalence point. *It is displaced about* **3** mols.% to the acid side, which is also *the side of higher viscosity.* This behaviour recalls the displacement of the maximum surface tension from the point of equivalence in the case of the salts from *iso*valeric to octoic acid. Hence, similar results are observed in the net effects upon σ and η of all the factors which are supposed to operate in the system, *i.e.*, formation of salts, molecular aggregates, dissociation, and the independent influence of each component according to some " mixture law."

Only viscosities being now considered, it is desirable to give a brief account of the work on and interpretation of viscosity maxima in binary mixtures. The simple view taken by Graham (*Phil. Trans.*, 1861, **151**, 373), that a maximum in the viscosity–composition curve definitely indicated the existence of a compound and established its composition, is now considered to be far too explicit, although it may be true in particular cases. The position was reviewed by Thole, Mussell, and Dunstan (J., 1913, **103**, 1108), who showed that associated liquids in general, and hydroxylated liquids in particular, have relatively high viscosities, and that maxima in the curves imply association, proceeding in the direction of complex formation. With regard to the system base–weak acid, there is much evidence that maxima occur usually on the acid side of the salt composition. This is true of aniline and acetic acid (*idem, ibid.*), and in the analogous case of *o*-toluidine–acetic acid the maximum lies at 72 mols.% of acid (Trifonow *et al.*, *loc. cit.*). In the systems aniline–*m*-cresol and toluidine–*m*-cresol, it lies at 65 mols.% of cresol; for pyridine with acetic and butyric acids at 77·9 and 74·4 mols.% respectively, *i.e.*, approximately 4 mols. of acid to 1 of pyridine (Tsakalotos, *Bull. Soc. chim.*, 1908, **3**, 234). Indeed, it was pointed out by Faust (*Z. physikal. Chem.*, 1912, **79**, 97) that there is always a maximum when the constituent liquids are acid and base, but that the composition of a compound cannot be deduced from this, since it frequently alters with the temperature and depends on the relative viscosities of the components. This effect was stressed by Tammann and Pillsbury (*Z. anorg. Chem.*, 1928, **172**, 143), who divided viscosity isotherms into four main groups. In the case of a weak acid with a weak base, maxima are found, but are displaced towards the composition of the component having the higher viscosity; *e.g.*, aniline–*o*-chlorophenol has a maximum at 54 mols.% of aniline, and phenol–aniline at 62 mols.% of phenol. Since these compounds are strongly dissociated in the liquid state, these displacements are to be expected. The same is true of salts of guaiacol with aniline, pyridine, etc. (Puschin and Pinter, *Z. physikal. Chem.*, 1929, *A*, **142**, 211). It thus appears to be the exception rather than the rule for the maximum to fall exactly at the salt composition, and the fact that it lies closer than usual in the present case indicates a higher degree of combination, both molecular and electrolytic, than in the cases previously investigated.

FIG. 3.

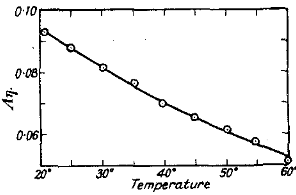


Variation of $\Lambda\eta$ *with Composition.*—Values of η were interpolated from the viscosity curve, and used to calculate the product $\Lambda\eta$ given in col. 4 of Table III: the curve for the latter function differs considerably from that for Λ, as is shown by Fig. 3. The two maxima in the Λ curve are evidently due to the fact that, up to these points on each side of the salt composition, increase in the mobilities of the ions more than compensates for diminution in their concentration. There is a new single maximum, which represents the maximum of concentration $\times$ mobility. It will be observed that this is slightly on the acid side, *i.e.*, 55 mols.% of acid. If the maximum of ionisation and also the maximum of viscosity were exactly at the equivalence point, the $\Lambda\eta$ curve would fall on either side. Actually, however, Λ is increasing, and also η is increasing for a short distance in the acid side. This can only mean that concentration as well as the mobility of the ions is increased by an excess of acid. This is also shown by the fact that, in the Λ curve, the acid maximum is much higher than the base maximum, in spite of the fact that the viscosity of a mixture containing

excess of base, *e.g.*, 40 mols. % of acid, is much lower than that of a corresponding mixture with excess of acid (60 mols. % acid). This seems to point to a greatly increased electrolytic dissociation due to either (*a*) increased ionising power of the acid considered as a medium, (*b*) repression of molecular dissociation of the salt, which is principally due to the weakness of the acid, or (*c*) formation of an acid salt which gives more dissociated ions than the stoicheiometrical salt. With regard to (*b*), it may be noted that, although the molecular dissociation of an anhydrous fused salt may appear to be symmetrical: $BH^+A^- \rightleftharpoons B + HA$, yet it is the proton affinities of the acid anion and the anhydro-base which determine the dissociation. If both have high proton affinities (weak acid), molecular dissociation will be extensive; on the other hand, if the proton affinity of the anion is low (strong acid), and that of the anhydro-base is high, molecular dissociation will be slight and electrolytic dissociation extensive: $BH^+A^- \rightleftharpoons BH^+ + A^-$. Condition (*c*) shows the dissociation of an acid salt derived by addition of the acid to an ampholyte type which is itself ionised but not dissociated, thus: $BH^+A^- + HA \rightleftharpoons BH_2A^+ + A^-$.

Variation of $\Lambda\eta$ *with Temperature.*—The constancy or otherwise of the product $\Lambda\eta$ with variation of temperature affords another basis of comparison between these salts and other fused salts. Materials for such comparison have been collected by Walden, Ulich, and Birr (*loc. cit*). According to the Stokes–Einstein law, the mobilities of ions are proportional to the expression $1/\eta r$ in which r is the radius of the ion. This is not exactly obeyed by aqueous electrolytes, although the agreement is better at higher temperatures. It cannot be expected to hold strictly for fused electrolytes, since (1) mutual effects of the ions on one another alter with temperature, and (2) the degree of dissociation of many salts may alter with temperature. Since the dissociation of the picrates of the tetrasubstituted bases is considered to be complete at all temperatures, variation (2) should be negligible, and picrates of quaternary bases should show more constant values of $\Lambda\eta$. Actually, this product was found to be fairly constant in salts such as tetra-amylammonium picrate, although an even better constancy is found with one or two partially substituted compounds such as diethylammonium picrate.

FIG. 4.



Piperidinium heptoate, whose variation of conductivity with temperature had been determined, was employed in this experiment. The thermostat was regulated by hand to ± 0·02°. Densities were interpolated from previous results. Observed values are shown below:

Temp.	17·6°	25·0°	30·1°	34·9°	39·9°	44·8°	49·7°	54·8°	59·7°
η	2·392	1·404	1·036	0·772	0·577	0·441	0·352	0·274	0·217

The variation of viscosity with temperature can be accurately expressed by the equation $\log \eta = 676{\cdot}0/(T - 144{\cdot}6) - 4{\cdot}252$, where T is the absolute temperature. This is therefore in accordance with Andrade's general formula for associated liquids (*Nature*, 1930, **125**, 309), *viz.*, $\log \eta = \beta/(T - \theta) + \alpha$. The simple formula $\log \eta = \beta/T + \alpha$, proposed for unassociated liquids, was shown by Prasad (*Phil. Mag.*, 1933, **16**, 263) to hold for the fused salts sodium and potassium nitrates and lead bromide, whereas for lead chloride the introduction of the constant θ was necessary. This was attributed to incomplete association at lower temperatures, so that piperidinium heptoate in this respect belongs to the class of only partly dissociated salts represented by lead chloride.

Values of η were interpolated from the curve and used to calculate the product $\Lambda\eta$, included in line 4 of Table II and shown in Fig. 4: $\Lambda\eta$ is far from constant, but falls considerably with rise of temperature. It resembles in form rather the $\Lambda\eta$ curve of many fused salts, *e.g.*, sodium and potassium chlorides, but lies at a lower level, and has an even smaller value than most of the fused picrates already referred to. Owing to the nature of the curves

of these salts, it was possible to extrapolate to a limiting value of about 0·36—0·42. Such extrapolation is not possible in the present case. It was noted that in general the salts of quaternary bases had the highest values; then followed the primary, the secondary, and finally the tertiary. There is therefore a superficial similarity in this respect between the piperidine salts and the tertiary ammonium picrates. Likewise, when comparison is made between the molar conductivities of the picrates and the heptoate under such conditions of temperature that all salts have the same viscosity, then the salt of the tertiary base, piperidine, shows a value resembling most closely those of the tertiary ammonium bases. It has been noted already that Walden considers the low Λ values of the salts of these bases to be due to less complete dissociation, and substitution of a weaker fatty acid for picric acid may still further reduce the dissociation. The values for the picrates are approximate only, obtained by the interpolation of Walden's results:

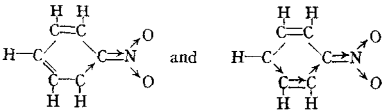
Salt.	η.	*t*.	Λ.
Piperidinium heptoate	0·214	60°	0·0627
Triamylammonium picrate	0·2165	120	0·197
Propylammonium picrate	0·21	127	1·45
Diethyldipropylammonium picrate	0·21	117	2·62

University College, Nottingham. [*Received, November 7th*, 1936.]

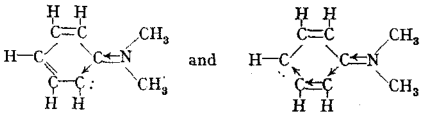
3. *An Investigation of Steric Influences on the Phenomenon of Mesomerism.*

By R. H. Birtles and G. C. Hampson.

The first physical evidence for the existence of permanent "electromeric" or "mesomeric" effects in unsaturated compounds came from the work of Sutton (*Proc. Roy. Soc.*, 1931, *A*, **133**, 668), in which he correlated the differences between the electric moments of aromatic and tertiary aliphatic compounds with the directive influences of the respective groups in aromatic substitution. As regards physical interpretation, it was later suggested that this phenomenon arose as a result of wave-mechanical resonance between different structures (Sutton, *Trans. Faraday Soc.*, 1934, **30**, 789; Ingold, *Chem. Reviews*, 1934, **15**, 225; Kumler and Porter, *J. Amer. Chem. Soc.*, 1934, **56**, 2549). For example, each molecule of nitrobenzene is considered to be a resonance hybrid between the normal molecule and structures of the type

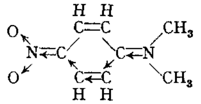


Opposite mesomeric effects occur with *o*, *p*-directing groups such as the dimethylamino-group:



In *p*-disubstituted benzene derivatives the mesomeric effects of the two para-groups may reinforce or oppose each other. This is revealed by the fact that the electric moment of a *p*-disubstituted benzene compound A— —B is not always the vector sum of

the moments of the two monosubstituted derivatives —A and —B. The degree of deviation varies with the nature of the groups A and B, two groups of opposite type showing the greatest deviation (see Marsden and Sutton, J., **1936**, 599, and references therein). An extreme case is *p*-nitrodimethylaniline, where the mutual reinforcement of the mesomerism is so great that the moment, 6·87, of the compound is very much greater than the sum of the moments of nitrobenzene, 3·95, and dimethylaniline, 1·58 (all moments in this paper are given in Debye units), even although these two component moments are not collinear (*idem, ibid.*).



If the above type of structure is really important there should be two further consequences : (1) The bond joining the group to the benzene ring should be shorter than the normal single-bond distance (Pauling, *Proc. Nat. Acad. Sci.*, 1932, **18**, 293, 498; Brockway, *ibid.*, 1933, **19**, 303, 868; Brockway and Pauling, *ibid.*, p. 860). (2) With groups such as NO_2, NH_2, NMe_2 or OMe there should be a tendency for the oxygen, hydrogen and methyl groups respectively to be brought into, and held in, the plane of the benzene ring. This follows from simple ideas of stereochemistry, based on tetrahedral atomic models.

If now we consider an aromatic compound in which two methyl groups have been substituted in the *o*, *o'*-positions to the polar group, the establishment of conditions (1) and (2) will be impeded for steric reasons. Hence the introduction of the *o*-methyl groups should reduce the probability of the quinonoid type of structure, and consequently the " mesomeric moment " should be diminished.

To test the theory we have measured the electric moments of a number of mono- and di-substituted derivatives of durene, and the results are shown in Table I together with those for the corresponding derivatives of benzene. The latter were taken from the " Table of Dipole Moments " by Sidgwick and collaborators (*Trans. Faraday Soc.*, 1934, **30**, Appendix).

TABLE I.

				Diff.
Nitrodurene	3·39	Nitrobenzene	3·95	0·56
Aminodurene	1·39	Aniline	1·53	0·14
Bromodurene	1·55	Bromobenzene	1·52	0·03
Nitroaminodurene	4·98	*p*-Nitroaniline	6·10	1·12
Bromoaminodurene	2·75	*p*-Bromoaniline	2·93	0·18
Bromonitrodurene	2·36	*p*-Bromonitrobenzene	2·65	0·29
Pentamethylaniline	1·10	*p*-Toluidine	1·36	0·26
Dinitrodurene	0·60	*p*-Dinitrobenzene	0·60	0·00

We will consider first the three monosubstituted derivatives. The moments of nitrodurene and aminodurene differ considerably from those of nitrobenzene and aniline, whereas the moments of bromodurene and bromobenzene are essentially the same. The differences between the moments of the durene compounds and those of the corresponding benzene compounds may be due to one or both of two causes; either the mesomeric effect in the durene compounds is reduced as predicted by the above theory, or the polar group sets up induced moments in the methyl groups of the durene molecule. The changes in moment are in the sense required by the former explanation, for the moments of the nitro- and the amino-durenes are intermediate between those of the corresponding benzene and aliphatic compounds (aliphatic nitro-compounds have moments of *ca.* 3·1, Hunter and Partington, J., **1933**, 309; and methylamine one of 1·23, Steiger, *Helv. Physica Acta*, 1930, **3**, 161; *Physikal. Z.*, 1931, **32**, 425). If the induction effect were the sole explanation, it is difficult to see why the effects in the cases of aminodurene and bromodurene should be of opposite kinds.

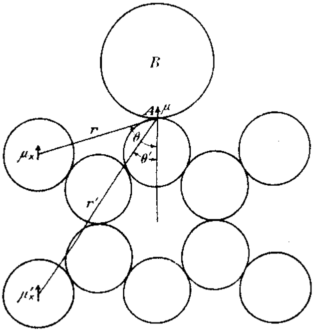
An attempt has been made to estimate the inducing influence of the polar group by the

method used by Hampson and Weissberger in the case of the chloronaphthalenes (J., 1936, 393). In these calculations a number of approximations and assumptions have to be made. For example, in addition to the difficulty of locating the position of the inducing dipole, the expression $\mu' = \frac{\varepsilon + 2}{3} \cdot \frac{\alpha c \mu}{\varepsilon r^3}$ only holds for values of r greater than about 3·5 A., *i.e.*, values for which the finite length of the dipole can be neglected.*

For the purposes of the calculation, the dipole has usually been located at the point of contact of the two component atoms of the polar bond (Smallwood and Herzfeld, *J. Amer. Chem. Soc.*, 1930, **52**, 1919; Hampson and Weissberger, *loc. cit.*), but since in the durene compounds it is found that the induced moments are very sensitive to the exact location of the inducing dipole, values have been worked out for various positions.

We will first consider the case of bromodurene, with the dipole located at the point of contact A of the carbon and bromine atoms (see figure).

The induced moment μ_x parallel to the inducing dipole is given by the expression $\mu_x = [(\varepsilon + 2)/3]\alpha\mu(3 \cos^2 \theta - 1)/\varepsilon r^3$. Using as standard data throughout, $\varepsilon = 2{\cdot}27$, $\mu = 1{\cdot}52 \times 10^{-18}$, $\alpha = 1{\cdot}82 \times 10^{-24}$, $C_{ar.}$–$C_{ar.}$ = 1·40 A., and $C_{ar.}$–$C_{al.}$ = 1·47 A., we obtain results shown in the top row of Table II. Hence on this hypothesis the moment of bromodurene should be 1·52 + 2(0·02 − 0·08) = 1·40.



If, instead, we locate the dipole at B, the centre of the bromine atom, the results are given in the second row of Table II, leading to a calculated moment in this case of 1·56. These two cases probably represent extreme limits.

In nitrodurene and aminodurene the inducing dipoles are themselves composite, being the resultant of the three bond moments about the nitrogen atom, and the location of this resultant is still more uncertain. Since, however, the moment of the bond between the nitrogen atom and the benzene ring will be less than the other two bond moments, qualitatively, at any rate, we may take as our limits (*a*) the case where the resultant is assumed to be at the centre of the nitrogen atom, (*b*) when it is located on the periphery of the nitrogen atom remote from the benzene ring.

TABLE II.

	r.	r'.	θ.	θ'.	μ_x.	μ'_x.	$\mu_{calc.}$
Dipole at point of contact of C and Br atoms	2·57	4·32	75°	35°	−0·08	+0·02	1·40
Dipole at centre of Br atom	3·10	5·33	53° 24′	27° 48′	+0·004	+0·015	1·56

The calculations then show that for case (*a*) the moments of nitrodurene and aminodurene should be the same as those of nitrobenzene and aniline, while for case (*b*) they should be considerably larger. Since, however, the moments of the durene compounds are *smaller* than those of the corresponding benzene compounds, it follows that these differences cannot be due solely to induced effects in the methyl groups, and that some other influence

* μ' is the induced dipole; ε is the dielectric constant across the part of the material in which the induction occurs; this is taken as the same as the dielectric constant of the material in bulk. α is the polarisability and may be deduced from the electronic polarisation term corresponding to that part of the molecule (assumed to be spherically symmetrical) in which the effect is being calculated, using the Debye equation $\alpha = 3P_E/4\pi N$; μ is the moment of the inducing dipole, r is the distance from this dipole to the polarisable centre, and c is an orientation factor (Frank, *Proc. Roy. Soc.*, 1935, *A*, **152**, 171).

is operative. This, as we have seen, must be a damping of the resonance due to the steric effect of the methyl groups.

With bromodurene no such effect is observed, nor is it to be expected, since here the ortho-methyl groups will only exert a steric influence by virtue of condition (1) (p. 11), and this would be but a feeble influence in comparison with condition (2).

Turning now to the disubstituted derivatives, we again observe (Table I) that the durene compounds have lower moments than the corresponding benzene compounds. This is especially marked in the case of the nitroamino-derivatives where the difference between the moments of the benzene and the durene compounds is 1·12. The moment of the amino-group is not, of course, coaxial with the benzene ring and hence, assuming vector addition, we should expect the moment of nitroaminodurene to be less than the algebraic sum of the moments of nitrodurene and aminodurene. The observed moment (4·98) in fact exceeds this sum (3·39 + 1·39) by an amount 0·20, but not by so much as the moment of *p*-nitroaniline exceeds the sum of the moments of nitrobenzene and aniline, *viz.*, 6·1 − (3·95 + 1·53) = 0·62. It is clear, therefore, that even in the durene compounds there is some interaction between the para-groups. In other words, the conclusion seems to be that in the monosubstituted durenes the mesomerism is reduced by the steric effect of the methyl groups, but that in the disubstituted durenes the two para-groups can bring about a mutual stabilisation of the quinonoid form though not to such a large extent as in the benzene compounds.

Another disubstituted durene compound which might be considered is that in which only one of the substituents is sterically influenced by the methyl groups; such a case is bromonitrodurene. Here the difference between observed (2·36) and calculated (3·39 − 1·55 = 1·84) moments is 0·52 and is greater than the corresponding difference (0·22) for *p*-bromonitrobenzene. A possible explanation is as follows:

In nitrodurene the mesomerism is reduced by a steric effect, but the introduction of a bromine atom, with its donating power into the ring, may partially overcome the steric effect and increase the importance of the quinonoid form. This interaction between the para-groups will cause the moment to be greater than the vector sum of the moments of nitrodurene and bromodurene. In nitrobenzene there is no such steric effect, and though the introduction of a para-bromine atom appears to bring about a further stabilisation of the quinonoid form, the interaction moment may not be so large as with the durene compound.

The moment (0·60) of dinitrodurene is in complete agreement with the small moments found for other symmetrical polynitro-compounds (H. O. Jenkins, J., 1936, 862).

Experimental.

Preparation and Purification of Materials.—Durene. Some of the durene was supplied by the Eastman Kodak Co. of Rochester, N.Y.; the rest was prepared from crude xylene by the Friedel–Crafts reaction with aluminium chloride and methyl chloride according to Smith's method ("Organic Syntheses," 1930, **10**, 32). The crude mixture of xylenes and tri-, tetra-, penta-, and hexa-methylbenzenes which is obtained was twice fractionated, and the durene was isolated from the fraction of range 180—205° by freezing it out in an ice–calcium chloride mixture and filtering it off. Finally it was recrystallised from alcohol; m.p. 79—80° (Smith, *loc. cit.*, 79—80°).

Dinitrodurene. Smith's method (*op. cit.*, p. 40) was used. A solution of 13·4 g. of durene in 150 c.c. of chloroform was added to 75 c.c. of concentrated sulphuric acid, the mixture cooled, and slowly nitrated with 6 g. of fuming nitric acid (*d* 1·5) with stirring, the temperature being kept below 50°. The acid layer was removed, and the chloroform layer washed with sodium carbonate solution and dried. Most of the chloroform was then distilled off, and the dinitrodurene obtained as white crystals by pouring into 250 c.c. of warm alcohol. Recrystallisation from alcohol gave a product, m. p. 207·5° (Smith, *loc. cit.*, 207—208°).

Nitroaminodurene. 3 G. of dinitrodurene were dissolved in 180 c.c. of boiling alcohol and to this solution, which was kept boiling and mechanically stirred, was added gradually an aqueous solution of 1·5 g. of sodium disulphide (prepared by dissolving 3·2 g. of $Na_2S,9H_2O$ in about 20 c.c. of water and warming with 0·45 g. of flowers of sulphur). After this addition the solution was stirred at its b. p. for a further 2 hours, excess alcohol evaporated off, and the remaining solution poured into cold water. The yellow precipitate was filtered off, washed with water, and

heated with a large amount of dilute hydrochloric acid. The mixture was then filtered, to remove any sulphur or unchanged dinitrodurene, and ammonia added to the filtrate. The orange precipitate was filtered off and dried; m. p. 156—158°; yield about 0·5 g., but about 2 g. of unchanged dinitrodurene, contaminated with sulphur, were recovered. The experiment was repeated with different amounts of sodium disulphide but no increase in yield was found. It was finally decided to treat the recovered dinitrodurene with more sodium disulphide solution and repeat the experiment several times in this way. Thus 15 g. of dinitrodurene gave 8 g. of nitroaminodurene together with 3·3 g. of unchanged dinitrodurene; recrystallised from alcohol, it had m. p. 161—162° (Cain, *Ber.*, 1895, **28**, 968, gives m. p. 158—159°). *Nitrodurene.* This was prepared according to Cain (*P.*, 1909, 260). 4·5 G. of nitroaminodurene were dissolved in alcohol 4—5 g. of concentrated sulphuric acid added with shaking and cooling, and the mixture diazotised with 2—3 g. of sodium nitrite. The mixture was then heated on a water-bath to remove nitrogen, most of the alcohol evaporated off, a little water added, and the mixture steam-distilled. At first alcohol came over, and then a whitish oil which solidified in the receiver. This was filtered off and dried. Recrystallisation from alcohol gave a pale yellow solid, m. p. 68·8—69·8° (Cain, *loc. cit.*, gives m. p. 70°).

Bromodurene. This was prepared from durene by the method of Smith and Moyle (*J. Amer. Chem. Soc.*, 1933, **55**, 1676), the crude product being purified by steam-distillation and recrystallisation from alcohol; m. p. 60° (Smith and Moyle, *loc. cit.*, give m. p. 60·5°).

Bromonitrodurene. Bromodurene was nitrated in chloroform solution with a mixture of concentrated sulphuric and fuming nitric acids as described by Smith and Tenenbaum (*J. Amer. Chem. Soc.*, 1935, **57**, 1293). Recrystallisation from alcohol gave white crystals, m. p. 179·2—180·2° (Smith and Tenenbaum give m. p. 179—181°).

Aminodurene. Willstätter (*Ber.*, 1909, **42**, 4159) reduced bromonitrodurene with zinc and acetic acid, but we obtained a better yield (80%) by reducing it with tin and hydrochloric acid in acetic acid solution. 4 G. of bromonitrodurene were dissolved in boiling glacial acetic acid 39 c.c. of concentrated hydrochloric acid added, and then, slowly, 6 g. of granulated tin. The solution was refluxed for several hours, then treated with a large quantity of concentrated sodium hydroxide solution and steam-distilled. A whitish oil solidified to a white solid in the receiver. This was filtered off and dried, and purified by sublimation in a vacuum and recrystallisation from ligroin (b. p. 60—80°); m. p. 72° (Willstätter gives m. p. 75°; Smith and Tenenbaum, *loc. cit.*, m. p. 71—73°).

Bromoaminodurene. 3·5 G. of aminodurene were dissolved in 25 c.c. of glacial acetic acid, and 3·5 g. of bromine in 20 c.c. of glacial acetic acid were slowly added. A white precipitate was immediately formed, which was filtered off, washed with a little acetic acid, and then suspended in water and ammonia added. The base was filtered off, dried, and crystallised from ligroin (b. p. 80—100°); 2·5 g. crystallised (m. p. 137·5—138·5°) and then a further crop of 1 g. (m. p. 135·5—137·5°) was got by cooling the mother-liquor in ice and salt. The latter crop after sublimation in a vacuum had m. p. 138·5—139·5°. Finally the whole was recrystallised from ligroin (b. p. 80—100°); m. p. 138·5—139·5° (Found: C, 53·0; H, 6·1; N, 6·2; Br, 35·1. Calc. for $C_{10}H_{14}NBr$: C, 52·6; H, 6·2; N, 6·1; Br, 35·1%).

Pentamethylaniline. This was prepared by essentially the same method as that described by Dimroth, Leichtlin, and Friedemann (*Ber.*, 1917, **50**, 1543), but aminodurene hydrochloride was used instead of *m*-5-xylidine hydrochloride as the starting material. 12 G. of aminodurene hydrochloride were heated with 2 g. of absolute methyl alcohol in a sealed tube for 8 hours at 250°, and the reaction products worked up in the manner described by Dimroth, Leichtlin, and Friedemann; 3 g. of pentamethylaniline, m. p. 152—153°, were obtained (Dimroth, Leichtlin, and Friedemann give 151—152°).

Measurements.—The data for the determination of dipole moments are in the following tables, where the symbols have their usual significance. All the measurements were carried out in benzene solution at 25·0°.

SUMMARY.

It is suggested that if the discrepancies between the observed dipole moments of *p*-disubstituted benzenes and those calculated assuming vector addition are due to resonance involving quinonoid structures, then with substituents such as NO_2, NH_2, NMe_2, and OMe there should be a tendency for the oxygen, hydrogen and methyl groups respectively to be held in the plane of the benzene ring. The introduction of methyl groups in the *o*-positions into these substituents would, on the other hand, exert a steric effect in forcing these three groups out of the plane of the benzene ring.

f_2.	$d_{4°}^{25°}$.	ϵ.	n^2.	P_2.	$_EP_2$.
			Nitrodurene.		
0·003706	0·8752	2·3348	2·2588	291·4	55·9
0·003192	0·8750	2·3266	2·2584	294·5	55·0
		$_{A+O}P_2 = 294{\cdot}5 - 55{\cdot}5 = 239$ c.c.; $\mu = 3{\cdot}39$.			
			Aminodurene.		
0·012234	0·8757	—	2·2608	—	49·7
0·009543	0·8752	—	2·2598	—	49·5
0·006188	0·8746	2·2904	—	87·9	—
0·003872	0·8742	2·2841	—	89·5	—
0·003247	0·8741	2·2823	—	89·1	—
		$_{A+O}P_2 = 89{\cdot}6 - 49{\cdot}6 = 40$ c.c.; $\mu = 1{\cdot}39$.			
			Bromodurene.		
0·016197	0·8857	2·3321	2·2610	103·4	53·1
0·013553	0·8837	2·3222	2·2619	103·1	54·8
0·009479	0·8806	2·3071	2·2590	103·3	53·1
0·004717	0·8771	2·2888	2·2575	100·1	51·9
		$_{A+O}P_2 = 103{\cdot}3 - 53{\cdot}2 = 50{\cdot}1$ c.c.; $\mu = 1{\cdot}55$.			
			Nitroaminodurene.		
0·007850	0·8777	2·5507	2·2608	541·5	56·7
0·007461	0·8775	2·5355	2·2604	540·6	57·1
0·006023	0·8768	2·4853	2·2602	546·1	57·0
0·002912	0·8752	2·3760	2·2589	559·9	58·6
		$_{A+O}P_2 = 572 - 57 = 515$ c.c.; $\mu = 4{\cdot}98$.			
			Bromoaminodurene.		
0·008612	0·8816	2·3693	2·2620	211·8	57·6
0·006308	0·8795	2·3431	2·2607	211·7	57·6
0·004847	0·8782	2·3274	—	213·9	—
		$_{A+O}P_2 = 214 - 57{\cdot}6 = 156{\cdot}4$ c.c.; $\mu = 2{\cdot}75$.			
			Bromonitrodurene.		
0·012951	0·8885	2·3806	2·2649	173·2	61·3
0·011839	0·8871	2·3707	2·2644	172·7	61·8
0·006760	0·8812	2·3296	2·2610	175·9	61·9
0·004721	0·8789	2·3125	2·2600	176·0	62·9
		$_{A+O}P_2 = 178 - 62 = 116$ c.c.; $\mu = 2{\cdot}36$.			
			Pentamethylaniline.		
0·010447	0·8758	2·2938	2·2605	79·2	53·9
0·007045	0·8750	2·2866	2·2594	79·0	54·4
		$_{A+O}P_2 = 79 - 54 = 25$ c.c.; $\mu = 1{\cdot}10$.			
			Dinitrodurene.		
0·024643	0·8919	2·2916	2·2639	64·7	57·0
0·022055	0·8899	2·2899	2·2629	64·9	56·8
0·014925	0·8846	2·2841	2·2619	64·2	57·2
0·010945	0·8816	2·2809	2·2602	64·8	57·3
		$_{A+O}P_2 = 64{\cdot}6 - 57{\cdot}1 = 7{\cdot}5$ c.c.; $\mu = 0{\cdot}60$.			

A number of durene compounds have been made and their electric moments measured. The latter are found to be lower than those of the corresponding benzene compounds, except in the case of bromodurene.

Since calculations show that the results cannot be explained by induced effects in the methyl groups, the conclusion is drawn that the lowering of moment is due to a damping of the resonance by the steric effect of the methyl groups. Bromodurene, on the other hand, has almost the same moment as bromobenzene, and here no steric influence is to be expected.

The moment of dinitrodurene (0·60) is in agreement with the small moments found for other symmetrical polynitro-compounds.

The authors wish to thank Prof. N. V. Sidgwick, Prof. L. Pauling, Dr. L. E. Sutton, and Dr. G. I. Jenkins for their help and interest in this work, and Imperial Chemical Industries Limited for a grant.

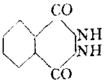
THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, November 20th, 1936.*]

4. *Chemiluminescent Organic Compounds. Part I. Isomeric Simple and Complex Hydrazides of Phthalic Acid and Mode of Formation of Phthalazine and* iso*Indole Rings.*

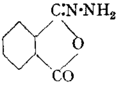
By H. D. K. Drew and H. H. Hatt.

Several classes of organic substances are chemiluminescent in presence of oxidising agents. The object of the work to be described in this series of papers is the further study of the chemistry of such substances and the ultimate application of its results to the luminescence problem. The *cyclo*phthalhydrazides (phthalaz-1 : 4-diones), a series showing notable chemiluminescent properties (Albrecht, *Z. physikal. Chem.*, 1928, **29**, 321), have first been studied.

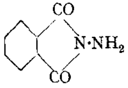
Condensation between hydrazine and phthalic anhydride was shown by Curtius and Fösterling (*J. pr. Chem.*, 1895, **51**, 371) to give phthalaz-1 : 4-dione (I), a substance also obtainable from phthalyl chloride or a phthalic ester and hydrazine hydrate (Davidis, *J. pr. Chem.*, 1896, **54**, 72). Rothenburg (*Ber.*, 1894, **27**, 691) prepared from phthalimide and hydrazine hydrate a different substance, to which he assigned structure (II); Curtius and Fösterling, however, regarded it as (III). A supposed third isomeride was obtained by Mihailescu and co-workers (*Bull. Acad. Sci. Roumaine*, 1923, **8**, 310; *Bul. Soc. Chim. România*, 1930, **12**, 95) from phthalic anhydride and hydrazine in acetic acid, and this also was given structure (III). Radulescu and collaborators (*Bull. Soc. chim.*, 1925, **37**,



(I.)



(II.)



(III.)

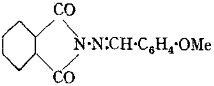
886; *Bul. Soc. Chim. România*, 1926, **8**, 117, 120, 137, 140) showed that Mihailescu's substance was identical with that of Curtius (I) and that Rothenburg's substance was spurious. On these grounds the more recent view has been held (*e.g.*, by Alexa and Gheorghiu, *Bull. Soc. chim.*, 1931, **49**, 112) that only the six-ring structure of *cyclo*phthalhydrazides is stable, the five-ring structures being either very unstable or incapable of formation.

This deduction is incorrect, however, since we now find that Rothenburg's condensation of phthalimide and hydrazine in alcoholic solution, although it yields only (I) if interaction is prolonged, gives a yield of some 50% of N-*aminophthalimide* (III) if the time is curtailed. *N*-Aminophthalimide has quite other properties than those recorded by Rothenburg for his material, which was doubtless a mixture of substances. It condenses readily with acetone and with benzaldehyde, the products being entirely different from those obtained by Rothenburg. At the melting point it changes completely into the six-ring structure (I). Nitrous acid converts it into phthalimide and nitrous oxide, a result which eliminates structure (II). Hydrolysis with acid, alkali, or boiling water brings about partial conversion into (I), though phthalic acid and hydrazine also are produced.

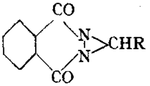
The ready convertibility of *N*-aminophthalimide into the six-ring hydrazide may be contrasted with the known behaviour of its *N*-substituted derivatives, where the change occurs only with difficulty: for example, *N*-phenylaminophthalimide is converted into 3-phenylphthalaz-1 : 4-dione only by heating for long periods in glycerol or with alcoholic sodium hydroxide (Chattaway and Tesh, J., 1920, **117**, 711).

The reverse transformation, that of a six- into the corresponding five-ring compound, has not hitherto been recorded in this series, but we have now observed an example: the condensation of Mihailescu's product, now known to be (I) but supposed by him to be (III), with *p*-anisaldehyde gave an anisylidene derivative to which he correctly (though for an incorrect reason) assigned formula (IV), and we find that it is identical with the product of the much more facile condensation between *N*-aminophthalimide and *p*-anis-

aldehyde. The six-ring compound, which cannot form a normal condensation product with an aldehyde or a ketone, is therefore changed into the five-ring compound under the influence of these reagents. In accordance with this, also, we find that, contrary to the



(IV.)



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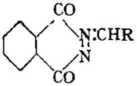
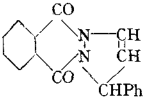
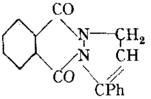


(VI.)

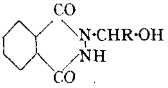
statements of a number of authors, the six-ring hydrazide (I) condenses slowly with benzaldehyde to give *N*-benzylideneaminophthalimide. The structures (V) and (VI) suggested by Radulescu (*loc. cit.*) for the anisylidene and cinnamylidene derivatives of (I) are in both cases erroneous, that of the anisylidene derivative for the reason already stated, and that of the cinnamylidene derivative owing to a further condensation which gives rise to the *3-phenyl-*1 : *2-phthalopyrazoline* (VII) or (VIII).



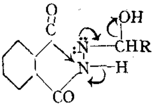
(VII.)



(VIII.)



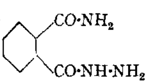
(IX.)



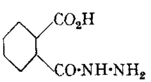
(IX*a*.)

This observation is of interest, since it affords evidence that the transformation of the six- into the five-ring occurs in all cases only after preliminary condensation with the aldehyde to give a substance of structure (IX). A probable mechanism for the molecular rearrangement involved in the change from (IX) to (IV), indicating a resemblance to the pinacol–pinacolin change, is shown in (IX*a*). In the case of cinnamaldehyde the further condensation at the double bond arrests the normal ring change. With (III), the condensation of cinnamaldehyde proceeds normally, to give the expected analogue of (IV).

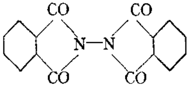
Following on the isolation of *N*-aminophthalimide, we re-examined in some detail the condensation of hydrazine with phthalimide and with phthalic anhydride. With phthalimide in alcoholic medium the first product was *o-carbamylbenzhydrazide* (X), which in boiling alcohol soon lost ammonia to give a mixture of *N*-aminophthalimide and the *cyclo*-hydrazide (I), the latter being present in part as its ammonium salt. When heated alone at 200°, (X) gave (I) together with hydrazine and phthalimide, so cyclisation evidently proceeds in three ways simultaneously.



(X.)



(XI.)

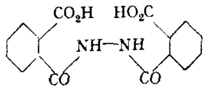
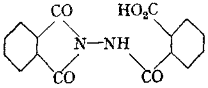


(XII.)

With phthalic anhydride and hydrazine in acetic acid, the evidence indicated that the half-hydrazide (XI) was the first product, though it was not isolated, and that it underwent cyclisation to (III) and (I) in the approximate ratio 3 : 2. Prolonged interaction of equimolecular quantities of hydrazine and phthalic anhydride in boiling acetic acid gave only (I), but if the reaction was stopped after only a few minutes, (III) was isolated in various proportions. When, however, an excess of phthalic anhydride was employed in the prolonged reaction, a mixture of (I) and N-*phthalimidophthalimide* (XII) was obtained, the yield of the latter being sometimes as high as 60%. Interaction of *N*-aminophthalimide with an excess of phthalic anhydride in acetic acid led to the quantitative production of (XII), a reaction which elucidates the structure of the latter and explains its formation in the foregoing condensation.

An obvious alternative mechanism for the production of (XII) in the above reaction

is the formation and self-condensation of s-*dibenzoylhydrazine*-2 : 2′-*dicarboxylic acid* (XIII), but this appears not to be utilised. The acid was synthesised through formation of its *methyl* ester from hydrazine and *o*-carbomethoxybenzoyl chloride in pyridine and subsequent hydrolysis of the ester. It is in part cyclised to (XII) when heated in acetic acid, but the yield of (XII) is actually smaller than that obtained in the direct condensation of hydrazine with phthalic anhydride in the same medium.

(XIII.)   (XIV.)

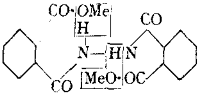
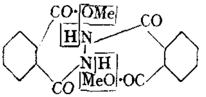
The *di*-N-*methyl* derivative of the methyl ester of (XIII) is unchanged by fusion, whereas the unsubstituted methyl ester cyclises quantitatively when heated.

All attempts to isolate (XIII) as a product of the reaction between hydrazine and two molecular proportions of phthalic anhydride failed, the first product being *N-phthalimido-phthalamic acid* (XIV); and this was the case also in the reaction between phthalic anhydride and *N*-aminophthalimide. It therefore seems proved that (XII) arises through preliminary formation of (III), and that the condensation between phthalic anhydride and hydrazine in acetic acid proceeds according to the scheme:

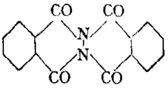
$$(XI) \xrightarrow{\text{cyclises}} (I) \xleftarrow{\text{rearranges}} (III) \xrightarrow[\text{anhydride}]{\text{phthalic}} (XIV) \xrightarrow{\text{cyclises}} (XII)$$

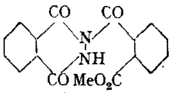
$$(XI) \xrightarrow{\text{cyclises}} (III)$$

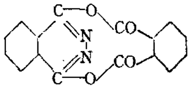
From the facts that the thermal cyclisation of (XIII), which probably proceeds through (XIV) as intermediate, leads to (XII) as the main product, and that (XII) is the sole product when the methyl ester of (XIII) is cyclised, it is obvious that cyclisation occurs in accordance with scheme (A), where the ester is formulated. The cyclisation can also be represented formally by scheme (B), which would lead to a product (XV) instead of

(A.)   (B.)

(XII). To supply further evidence that (XII) and not (XV) represents the structure of *N*-phthalimidophthalimide, this was synthesised by condensing *N*-aminophthalimide with *o*-carbomethoxybenzoyl chloride in presence of pyridine; the *methyl* ester of (XIV)


(XV.)


(XVI.)


(XVII.)

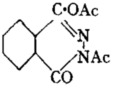
that resulted gave (XII) quantitatively on thermal cyclisation. That the preference for the formation of the di*iso*indole system [scheme (A)] is not due to lack of stability in compounds containing the double nitrogen bridge seems to be shown by the considerable stability of (VII); it is probably to be attributed to the steric disposition of the groups in such compounds as (XIII). The case recalls the preference for the formation of the di-indole rather than the alternative epindoline system noted by Robinson and Ainley (J., 1934, 1509) and other authors.

For the preparation of (XV), the obvious method of condensing (I) with phthalic acid was abortive, no reaction occurring, and although 2-*o-carbomethoxybenzoylphthalaz-1 : 4-dione* (XVI) was obtained by condensing (I) with *o*-carbomethoxybenzoyl chloride in pyridine, its thermal cyclisation was a complex process leading to (I) and (XII). Condens-

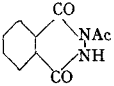
ation of *s*-phthalyl chloride with (I), however, led to the desired 2 : 3-*phthalophthalaz*-1 : 4-*dione* (XV). It is a crystalline, faintly yellow substance, sublimable under reduced pressure, and readily hydrolysed by dilute acid or alkali to phthalic acid and (I). Alternative structures, such as (XVII), derived from the enolised forms of (I), appear impossible or very improbable owing to strain, as may be seen from models; we attempted, however, to synthesise (XVII) by acting upon 1 : 4-dichlorophthalazine with phthalic acid and obtained only 4-chlorophthalaz-1-one, phthalic anhydride, and hydrogen chloride, indicating that the probable initial product, 4-chloro-1-phthalazyl hydrogen phthalate, fails to cyclise to (XVII). Again, only if structure (XV) were correct should the same compound result from the condensation of 5-nitrophthalaz-1 : 4-dione with phthalyl chloride on the one hand and of phthalaz-1 : 4-dione with 3-nitrophthalyl chloride on the other; actually, both condensations gave very similar mixtures, from which only (XV) was isolated, a result which is probably to be attributed to disproportionation of the initial unsymmetrical tetracyclic products. Similar results were obtained with the 6-nitro-compound; and the condensation of *s*-phthalyl chloride with diacetylhydrazine likewise gave rise to (XV).

The isomeric compounds (XII) and (XV) are of particular interest with regard to the stereochemistry of tervalent nitrogen.

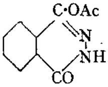
Whether *cyclo*phthalhydrazide should be represented by (I) or by the di- or the mono-enolic (lactim) form is still an open question. Radulescu (*loc. cit.*) adopted structure (I) for most purposes; but Rowe and Peters (J., 1933, 1331) represented the hydrazide as a dienol in acid or neutral solution and as a monoenol in alkaline solution, finding no support for structure (I). We consider that our experiments tend to support formula (I), especially the reaction with cinnamaldehyde, though obviously there is tautomerism. We have been unable to confirm the statement of Rowe and Peters that diacetylation leads to 1 : 4-diacetoxyphthalazine. They obtained the same monoacetyl derivative (m. p. 173°) both by direct acetylation with acetic anhydride–acetic acid and by partial hydrolysis of the diacetyl compound with alcohol. Repeating these experiments, we obtained two substances, which, although they have nearly the same melting point, melt at a lower temperature when mixed and are not identical. Since with acetic anhydride each gives the same known diacetyl derivative, this cannot be 1 : 4-diacetoxyphthalazine as supposed by Rowe and Peters, but must be 4-*acetoxy*-2-*acetylphthalaz*-1-*one* (XVIII). The two mono-



(XVIII.)



(XIX.)



(XX.)

acetyl derivatives are then (XIX) and (XX). The product of direct acetylation is identical with the monoacetyl derivative resulting from acetylation with acetyl chloride and pyridine. The reaction of diacetylhydrazine with phthalic anhydride takes an unexpected course, yielding N-*acetamidophthalimide* and acetic acid; and the same acetyl derivative is obtained when acethydrazide is used.

Experimental.

Phthalaz-1 : 4-*dione* (I).—Phthalic anhydride (14·8 g.) was refluxed for 4 hours with the requisite amount (Mihailescu and Floresco, *Bull. Acad. Sci. Roumaine*, 1923, 8, 310) of a solution of hydrazine sulphate and sodium acetate in dilute acetic acid. After cooling, the crystals were removed and washed with dilute acetic acid and water (yield, 9·7 g.); they melted at 333—336° and were completely soluble in aqueous ammonia. Concentration of the mother-liquor gave a second fraction (4·0 g.), of which 0·8 g. was insoluble in aqueous ammonia and consisted of nearly pure *N*-phthalimidophthalimide, m. p. 311—313° after crystallisation from acetic acid. The phthalaz-1 : 4-dione present in the ammoniacal liquors was precipitated by carbon dioxide or hydrochloric acid and recrystallised from alcohol, nitrobenzene, or acetic acid. The same material was also prepared from hydrazine hydrate and phthalic anhydride in alcohol (method of Fösterling, *loc. cit.*) and from hydrazine hydrate

and phthalimide by refluxing in alcohol for 6 hours (method of von Rothenburg, *loc. cit.*). All these products melted at 341—344° (corr.) with shrinkage from 320—324°. This manner of melting suggests that phthalaz-1 : 4-dione undergoes tautomeric change to the lactim shortly before melting.

N-Phthalimidophthalimide (XII).—Hydrazine hydrate (2 g.) in glacial acetic acid (20 c.c.) was added during ½ hour, with shaking, to a refluxing solution of phthalic anhydride (12 g.) in glacial acetic acid (40 c.c.). After 1 hour, the mixture was cooled, and the precipitate removed, washed, crushed, and digested for 2 hours with 400 c.c. of N/4-aqueous ammonia. The insoluble *N-phthalimidophthalimide* (5·25 g.), recrystallised from acetic acid, formed large colourless prisms, m. p. 311—313° (corr.), subliming at a slightly higher temperature (Found: C, 65·6; H, 2·8; N, 9·6; *M, in camphor*, 280, 285. $C_{16}H_8O_4N_2$ requires C, 65·75; H, 2·8; N, 9·6%; *M*, 292). On acidification the ammoniacal liquor gave 3·24 g. (50%) of phthalaz-1 : 4-dione. The yield of (XII) falls to 4·8 g. (41%) if the hydrazine solution is added in one lot and is raised to 6·6 g. (56%) if excess of phthalic anhydride (24—30 g.) is used. With alcohol, ether, and water as solvents, the yields were respectively 16, 13, and 1%. *N*-Phthalimidophthalimide is insoluble in water, sparingly soluble in alcohol and benzene, and readily in aniline. Its solubility in boiling acetic acid is 2·5 parts in 100. Hydrolysis with dilute sulphuric acid yields a mixture of (I) and phthalic acid.

Hydrolysis with hydrazine. *N*-Phthalimidophthalimide (0·50 g.) was added to a solution of hydrazine hydrate (0·2 g.) in glacial acetic acid (25 c.c.), and the mixture boiled for 1 hour. Excess of water was added, and the whole evaporated to dryness under reduced pressure: this process was repeated twice. The residues were treated with water (25 c.c.) containing a drop of hydrochloric acid; the insoluble material was pure phthalaz-1 : 4-dione (0·52 g.; calc., 0·55 g.). The formation of (XII) in the preparation of (I) in acetic acid may therefore be prevented by using a slight excess of hydrazine.

Hydrolysis with alkali. *N*-Phthalimidophthalimide (8·8 g.) and *N*-sodium hydroxide (100 c.c.) were refluxed together for 2 hours and ether was added to the ice-cold liquor, followed by 2*N*-sulphuric acid (53 c.c.). The colourless needles of *s*-dibenzoylhydrazine-2 : 2′-dicarboxylic acid (XIII) were collected after 10 minutes [prolonged standing leads to admixture with (I)], washed with water and ether, and dried over phosphoric oxide (yield, 8·4 g.). The acid lost water at 170—190° and melted at 260—305°. It was identical with the *s*-dibenzoylhydrazine-2 : 2′-dicarboxylic acid obtained by hydrolysis of its ester.

N-Aminophthalimide (III).—(1) Small and variable amounts of this substance result from short-period reaction between phthalic anhydride and hydrazine. To 96% hydrazine hydrate (4·3 c.c.) in acetic acid (50 c.c.) was added powdered phthalic anhydride (12 g.), and the mixture heated at once, with shaking, for 1—1½ minutes. A strong yellow colour developed, but a clear solution was never obtained. After rapid cooling, pouring into water (800 c.c.), and 1 hour's keeping, the precipitate was removed (A), and the filtrate left for 12 hours. Crude *N*-aminophthalimide (0·5—1·0 g.) separated; it crystallised from alcohol in faintly yellow needles, which melted at 200—205°, resolidified, and melted again at 338—341°. The material (A) was largely (I) with a little of (III) and (XII).

(2) 96% Hydrazine hydrate (4·4 g.) in 96% ethyl alcohol (80 c.c.) was treated with powdered phthalimide (12 g.), the mixture shaken for 2 minutes at room temperature, the resulting spongy mass quickly heated, and refluxed for 3 minutes (ammonia was evolved), water (50 c.c.) added at once, and the nearly clear solution added to water (200 c.c.). Pure *N-aminophthalimide* crystallised during an hour. It was recrystallised from 96% alcohol, in which it dissolved (1 part in 44 at b. p.) to form a yellow solution. Yield, 5·5—6·0 g. (Found: C, 59·3; H, 3·9; N, 17·4. $C_8H_6O_2N_2$ requires C, 59·3; H, 3·7; N, 17·3%). The aqueous filtrate on acidification gave about 6 g. of (I).

N-Aminophthalimide rapidly reduces Nessler's solution and warm Fehling's solution. It crystallises well from hot water, but at the same time undergoes a slow change; *e.g.*, 0·575 g., refluxed with water for 15 hours, left 0·48 g. of insoluble (I) and the solution contained hydrazine phthalate. The rearrangement to (I) is hastened and rendered quantitative by the presence of alkali; acids accelerate both rearrangement and decomposition. At its m. p. *N*-aminophthalimide is converted almost quantitatively into (I), but the latter contains about 1% of an unidentified yellow solid, removable through its insolubility in ammonia. *N*-Aminophthalimide is stable below its m. p. and can be sublimed under reduced pressure at 150°. It is stable in neutral alcoholic solution.

Action of potassium nitrite. *N*-Aminophthalimide (0·28 g.), suspended in glacial acetic acid (10 c.c.), was treated at room temperature with a concentrated aqueous solution of

potassium nitrite (0·2 g.). After an hour water was added in excess; the insoluble material (0·22 g.) melted at 230—231° and was identified as phthalimide.

N-*Acetamidophthalimide*, obtained by refluxing (III) with a little acetic anyhdride for a few minutes, formed colourless prismatic needles, m. p. 228—230°, from hot water (Found: C, 58·7; H, 3·7; N, 13·9. $C_{10}H_8O_3N_2$ requires C, 58·8; H, 3·9; N, 13·7%). *N*-Aminophthalimide on prolonged refluxing in acetic acid solution was converted into a mixture of its acetyl derivative with (I), (XII), and hydrazine. *N*-Acetamidophthalimide is only slightly changed by long boiling with water, but is hydrolysed by hot dilute mineral acid or alkali into acetic acid, phthalic acid, hydrazine, and (I).

N-iso*Propylideneaminophthalimide*.—*N*-Aminophthalimide (1 g.) and acetone (20 c.c.) were refluxed together for 2 hours, and the acetone removed in a vacuum. The dried residue was analytically pure (yield, 1·2 g.). After recrystallisation from aqueous acetone, it formed large colourless prisms, m. p. 97—100° (Found: C, 65·2; H, 5·2. $C_{11}H_{10}O_2N_2$ requires C, 65·3; H, 5·0%). Rothenburg gives m. p. above 260°. It was readily hydrolysed by water or aqueous alcohol to acetone (identified as dibenzylideneacetone), *N*-aminophthalimide, and hydrazine phthalate.

N-*Benzylideneaminophthalimide*, prepared by refluxing benzaldehyde (1 g.), *N*-aminophthalimide (1 g.), and 96% alcohol (25 c.c.) for 1 hour, separated overnight in colourless needles, m. p. 166—167°, unchanged by recrystallisation (Found: C, 72·15; H, 4·5; N, 11·3. $C_{15}H_{10}O_2N_2$ requires C, 72·0; H, 4·0; N, 11·2%). Rothenburg gives m. p. above 250°. The substance was slowly hydrolysed by boiling water, benzaldehyde (identified as benzylideneazine) distilling in the steam and the solution containing a mixture of (III), (I), hydrazine, and phthalic acid. Hydrolysis with hot *N*/10-sulphuric acid was rapid and led to a greater proportion of (I).

N-*p*-Anisylideneaminophthalimide (IV), similarly prepared from *N*-aminophthalimide (1 g.) and *p*-anisaldehyde (1 g.), was extracted from the separated crystals by means of benzene and recrystallised from alcohol, forming stout sulphur-yellow crystals, m. p. 189—191° (Found: C, 68·1; H, 4·8; N, 10·1. Calc. for $C_{16}H_{12}O_3N_2$: C, 68·5; H, 4·3; N, 10·0%). Water hydrolyses it slowly; dilute acids, rapidly.

N-*Cinnamylideneaminophthalimide* was similarly prepared from cinnamaldehyde (0·55 g.), *N*-aminophthalimide (0·5 g.), and 96% alcohol (20 c.c.). It separated on cooling and after recrystallisation from alcohol formed flocks of nearly colourless, hairy crystals, which invariably changed after a time into compact sulphur-yellow crystals: both varieties melted at 199—200° (Found for the yellow form: C, 73·9; H, 4·7; N, 10·1. $C_{17}H_{12}O_2N_2$ requires C, 73·9; H, 4·35; N, 10·1%). When the compound was heated with *N*/10-sulphuric acid in a current of steam, cinnamaldehyde (identified as cinnamylideneazine) distilled slowly, and (I), hydrazine and phthalic acid were left behind.

N-*Piperonylideneaminophthalimide* was obtained similarly from piperonal (1·1 g.), *N*-aminophthalimide (1 g.), and 96% alcohol (10 c.c.). It was precipitated from the cool filtered solution by the gradual addition of water. Crystallisation from benzene–alcohol gave sulphur-yellow needles (0·65 g.), m. p. 186·5—187° (Found: N, 9·8. $C_{16}H_{10}O_4N_2$ requires N, 9·5%).

o-*Carbamylbenzhydrazide* (X).—Powdered phthalimide (1·47 g.) in 99% alcohol (25 c.c.) was treated at 0° with a solution of hydrazine hydrate (0·5 g.) in 99% alcohol (10 c.c.). The mixture was shaken and watched under a microscope until phthalimide was no longer seen. After shaking at 0° for ½ hour, the colourless micro-crystals were removed, washed with alcohol and absolute ether, and dried in a vacuum over phosphoric oxide (Found: C, 53·95; H, 5·4; N, 23·4. $C_8H_9O_2N_3$ requires C, 53·65; H, 5·05; N, 23·45%). This *substance* reduced cold Nessler's and warm Fehling's solution. When heated, it lost ammonia, began to shrink at 220° and melted at 300—320° to a yellow liquid. When 0·5 g. of a specimen that had been kept 4 days was heated for 3 minutes in 4 c.c. of alcohol, ammonia was evolved and the product, when worked up as in the preparation of *N*-aminophthalimide (method 2), gave a 51% yield of this, the other product being (I). When heated in acetic acid with phthalic anhydride, (X) was converted to the extent of 35% into (XII).

When (X) (0·3764 g.) was heated at the boiling point of nitrobenzene in a current of nitrogen for 2 hours, ammonia and hydrazine were evolved: they were absorbed in dilute acid, and the hydrazine estimated by means of Fehling's solution (yield, 0·001 g.; 5%). The loss in weight was 0·0335 g. (calc. for maximum possible loss of ammonia, 0·0355 g.). The residue consisted of (I) and a small sublimate of phthalimide (m. p. 230—233°).

Condensation of Phthalaz-1 : 4-dione with Aldehydes*.—(A) *With benzaldehyde*. Phthal-

az-1 : 4-dione (2 g.) and benzaldehyde (10 g.) were refluxed together for 15 hours, the water evolved being allowed to escape. The brownish crystals which separated on cooling were removed, washed with ether (yield, 2·2 g.; m. p. 159—162°), and recrystallised from alcohol (charcoal), *N*-benzylideneaminophthalimide being obtained in colourless needles identical with the material prepared from (III).

(B) *With anisaldehyde.* Phthalaz-1 : 4-dione (2 g.) and anisaldehyde (10 c.c.) were refluxed together for 2 hours and the reddish paste was rubbed with ether, filtered, and washed with ether. Crystallised from alcohol, the product (2 g.) melted at 189—190° (Mihailescu and Florescu reported 188—190°) and was identical with the material prepared from (III).

3-Phenyl-1 : 2-phthalopyrazoline (VII or VIII).—Phthalaz-1 : 4-dione (12 g.) and freshly distilled cinnamaldehyde (20 c.c.) were mixed and heated rapidly to boiling over a naked flame for not more than 4 minutes. After cooling, the glue-like mass was crushed with ether, and the insoluble yellow powder washed with ether until free of resin. The resulting solid (12—14 g.) was extracted several times with hot chloroform (100 c.c. in all), leaving a white residue containing (I) and unidentified substances. The chloroform liquors gave the required *substance*, which formed sulphur-yellow crystals, m. p. 224—228°, from alcohol or chloroform–ether; it slowly turned green in bright light, was almost insoluble in ether, dissolved in about 90 parts of hot 96% alcohol, and was very soluble in chloroform (Found: C, 73·8; H, 4·3; N, 10·2. $C_{17}H_{12}O_2N_2$ requires C, 73·9; H, 4·35; N, 10·1%). When heated for several hours with dilute sulphuric acid in a current of steam, the substance evolved no cinnamaldehyde.

Action of alcoholic sodium ethoxide. 3-Phenyl-1 : 2-phthalopyrazoline (4 g.) was added to a solution of sodium ethoxide (9 g.) in 99% alcohol (70 c.c.), and the mixture refluxed for an hour in an atmosphere of nitrogen. A fuchsine colour developed and then faded to yellow, sodium phthalate separating (2·66 g.; calc., 3·04 g.). The alcoholic filtrate was evaporated several times with water under reduced pressure in an atmosphere of nitrogen; the oil that separated was extracted in chloroform (yield, 1·5 g.) and identified as 5-phenylpyrazoline, or an isomer, by conversion into 1-nitroso-5-phenylpyrazoline (von Auwers and Heimke, *Annalen*, 1927, **458**, 210), which formed buff micaceous plates, m. p. 157°, from methyl alcohol (Found: C, 61·1; H, 5·6; N, 23·4. Calc. for $C_9H_9ON_3$: C, 61·7; H, 5·1; N, 24·0%). It was identical with the nitroso-compound prepared from synthetic 5-phenylpyrazoline (Rothenburg, *Ber.*, 1894, **27**, 788; see also Knorr, *Ber.*, 1895, **28**, 688; *J. pr. Chem.*, 1896, **53**, 127). The isolation of 1-nitroso-5-phenylpyrazoline by nitrous acid treatment does not fix the position of the double bond in the phenylpyrazoline, since, owing to isomerisation, 3- and 5-phenylpyrazoline give the same nitroso-derivative.

The Action of Phthalic Anhydride on N-*Aminophthalimide.*—*N*-Aminophthalimide (0·48 g.) and phthalic anhydride (1·0 g.) were refluxed in acetic acid (5 c.c.) for 10 minutes. After cooling, and addition of water, the precipitate of *N*-phthalimidophthalimide (XII) obtained was washed with alcohol to remove phthalic acid; m. p. 311—313° after one crystallisation (yield, nearly quantitative). When *N*-aminophthalimide (0·8 g.) and phthalic anhydride (2 g.) were heated together at 160°, 1·32 g. of (XII) were obtained.

N-3′-*Nitrophthalimidophthalimide*, prepared by refluxing *N*-aminophthalimide (0·5 g.) and 3-nitrophthalic anhydride (1·2 g.) in acetic acid (5 c.c.) for 15 minutes, separated on cooling (yield, 1 g.); it was crushed with aqueous ammonia and crystallised from acetic acid, forming colourless hexagonal plates, m. p. 249—250° (Found: N, 12·9. $C_{16}H_7O_6N_3$ requires N, 12·5%). The condensation proceeds without solvent at 180—190°.

N-4′-*Nitrophthalimidophthalimide* (1·4 g.), similarly prepared from *N*-aminophthalimide (0·7 g.) and 4-nitrophthalic anhydride (1·5 g.), formed faintly yellow needles, m. p. 250°, from acetic acid (Found: N, 12·6%).

Methyl s-*Dibenzoylhydrazine-2 : 2′-dicarboxylate.*—8·3 G. of *o*-carbomethoxybenzoyl chloride (Meyer, *Monatsh.*, 1901, **22**, 277) were added to ice-cold pyridine (20 c.c.) with cooling. A spongy yellow mass was produced and the pyridine became red. Hydrazine hydrate (1 g.) in pyridine (10 c.c.) was then added, with cooling in ice and shaking. After warming at 40° for a few minutes, the solid dissolved. The mixture was left overnight, poured into water (400 c.c.) containing sufficient sulphuric acid to neutralise the pyridine, and left for 2—3 hours [longer standing leads to contamination with (I)]; the precipitate obtained crystallised from alcohol in colourless hair-like needles (Found: C, 60·8; H, 4·5; N, 8·1. $C_{18}H_{16}O_6N_2$ requires C, 60·7; H, 4·5; N, 7·9%). It melted between 180° and 200° according to the rate of heating, with evolution of gas and resolidification, melting again at 303—306°. *Methyl* s-*dibenzoylhydrazine-2 : 2′-dicarboxylate* is fairly readily soluble in acetone, readily soluble in acetic acid, but only slightly in water or ether.

Cyclisation.—(A) *By heat.* The ester (0·324 g.) was heated at 190—200° in a stream of carbon dioxide. On melting, the substance gave off a vapour, which was condensed in a freezing mixture. The residue was finally heated for a few minutes at 280°; pure *N*-phthalimidophthalimide, m. p. 311—313°, was obtained in theoretical amount. The condensate (0·054 g.; calc., 0·056 g.) was methyl alcohol, identified as methyl 3 : 5-dinitrobenzoate.

(B) *By acetic acid.* When the ester (0·324 g.) was heated in acetic acid for 4 hours, 0·257 g. of (XII) was obtained.

The ester reacts in a more complicated manner with mineral acids: heating with 0·1 *N*-sulphuric acid hydrolysed the ester into (XII) (yield, 30%), phthalic acid, and (I) (yield, 65%), together with some free hydrazine.

s-*Dibenzoylhydrazine*-2 : 2′-*dicarboxylic Acid* (XIII).—Treatment of the methyl ester with cold dilute aqueous alkali produces a light yellow solution (probably of the lactim sodium salt of the ester), from which immediate acidification precipitates much of the ester unchanged; but on standing the yellow colour quickly disappears and acidification then liberates the *dicarboxylic acid.* The methyl ester (0·47 g.) was shaken as a powder with 0·25*N*-sodium hydroxide (16 c.c.), and the solution kept till colourless. Ether was added, and dilute sulphuric acid until the mixture was acid to methyl-orange. The dicarboxylic acid separated mixed with a little of (I), which was removed by solution in 80% aqueous acetone and filtration; the filtrate, concentrated and precipitated by ether, gave the acid as colourless needles (0·3 g.). *It lost water between 170° and 190° and melted from 260—320°; it decomposed* aqueous sodium carbonate and was reprecipitated by acetic acid (Found: C, 58·5; H, 4·0; N, 8·7; equiv., by titration with barium hydroxide, 166. $C_{16}H_{12}O_6N_2$ requires C, 58·5; H, 3·7; N, 8·5%; equiv., 164). Heated on a bath of nitrobenzene, the acid lost water and gave a sublimate of phthalic anhydride, the residue consisting of a mixture of (XII), (I), and phthalic anhydride. In boiling acetic acid the acid decomposed, giving the same three products, the yield of (XII) being 30%. The *hydrazine* salt separated as a powder when the acid was warmed in alcohol with hydrazine hydrate (Found: C, 53·0; H, 4·8. $C_{16}H_{16}O_6N_4$ requires C, 53·3; H, 4·5%). The *silver* salt was obtained as light yellow crystals from the ammonium salt and silver nitrate in aqueous alcoholic solution; it was washed with alcohol and dried (Found: Ag, 40·6. $C_{16}H_{10}O_6N_2Ag_2$ requires Ag, 39·8%). The silver salt was shaken in a sealed tube with methyl iodide in dry benzene and after several days the insoluble material was removed and extracted with hot alcohol, which, on cooling, deposited hair-like crystals identified as methyl *s*-dibenzoylhydrazine-2 : 2′-dicarboxylate.

Methyl s-*Dibenzoyldimethylhydrazine*-2 : 2′-*dicarboxylate.*—To *o*-carbomethoxybenzoyl chloride (9·5 g.) in ice-cold pyridine (20 c.c.) was added, with shaking, a solution of *s*-dimethylhydrazine (1·4 g.) (Hatt, "Organic Syntheses," **16**, p. 18) in pyridine (12 c.c.). After a day the crystals of pyridine hydrochloride were removed, and the filtrate added to an excess of water; the solution gradually deposited very long, colourless, refractive prisms, which were recrystallised from 50% alcohol; m. p. 171—172° (Found: C, 62·7; H, 5·8; N, 7·6. $C_{20}H_{20}O_6N_2$ requires C, 62·5; H, 5·2; N, 7·3%).

N-*Phthalimidophthalamic Acid* (XIV).—A hot solution of phthalic anhydride (12 g.) in acetic acid (40 c.c.) was treated rapidly with hydrazine hydrate (2 g.) in acetic acid (20 c.c.). The mixture, refluxed for ½ minute, became yellow and a solid began to separate; the whole was quickly cooled and poured into 600 c.c. of water, and the precipitate collected after 1—2 hours, washed, and left overnight in 100 c.c. of 80% acetone. The undissolved material [chiefly (XII) and (I)] was removed, and the acetone filtrate concentrated at room temperature under reduced pressure, giving 2·5—3 g. of the crude *acid* as colourless plates; it was dried, dissolved in the calculated quantity of aqueous sodium carbonate, and the filtered solution precipitated with acetic acid; the acid was then dissolved in 80% aqueous acetone, and the filtered solution caused to crystallise by gradual addition of water. The acid was finally obtained in colourless hexagonal plates, which decomposed with loss of water at 160—190° and gave a residue of m. p. 307—310° (Found: C, 61·8; H, 3·9; N, 9·3. $C_{16}H_{10}O_5N_2$ requires C, 61·9; H, 3·3; N, 9·0%). It does not reduce Fehling's solution; it decomposes aqueous sodium carbonate, but more slowly than *s*-dibenzoylhydrazine-2 : 2′-dicarboxylic acid; it is also more soluble than the latter in 80% aqueous acetone. Cyclisation to (XII) was not quantitative at 200° and the amount of water produced was less than that calculated; the yield of (XII) was about 70%, the other products being (I) and phthalic anhydride. In hot acetic acid the cyclisation was quantitative only if an excess of phthalic anhydride was present; in its absence the products were those of the thermal decomposition, although the

yield of (XII) was higher (80%); no free hydrazine was produced. Aqueous sodium hydroxide brought about conversion into the sodium salt of (XIII).

Preparation from N-*aminophthalimide.* N-Aminophthalimide (1 g.) and phthalic anhydride (1 g.) were refluxed in acetic acid (10 c.c.) for ¾ minute; the mixture was then cooled and poured into excess of water. From the precipitate, N-phthalimidophthalamic acid (0·9 g.) was isolated as described above. The *silver* salt (white) was obtained from the ammonium salt and silver nitrate in aqueous alcohol (Found: Ag, 25·55. $C_{16}H_9O_5N_2Ag$ requires Ag, 25·9%).

Methyl N-*Phthalimidophthalamate.*—*o*-Carbomethoxybenzoyl chloride (5 g.) was added to ice-cold pyridine (15 c.c.) and treated at 0° with a mixture of N-aminophthalimide (3·5 g.) and pyridine (12 c.c.). The mixture was rubbed or shaken at 0° until the acyl chloride-pyridine addition compound had disappeared. Next day the precipitate of pyridine hydrochloride and (XII) was removed, and the filtrate poured into an excess of and made just acid. A mixture (5 g.), at first oily, of the desired *ester* and (XII) separated; this was dissolved in a little cold chloroform, the precipitate formed on addition of ether removed, and the filtrate further precipitated with more ether. The first precipitate was initially (XII), but after several repetitions of the process only the required ester separated (Found: C, 63·2; H, 3·9. $C_{17}H_{12}O_5N_2$ requires C, 63·0; H, 3·7%). The ester formed white microneedles, which melted with effervescence at 166—168°, re-solidified, and melted again at 310—313°, conversion into (XII) having taken place. When heated in a bath of boiling nitrobenzene, it lost methyl alcohol, identified as methyl 3 : 5-dinitrobenzoate (Found: loss in weight, 9·6. Calc., 9·9%). It was very soluble in hot organic solvents, but in all cases underwent some cyclisation to (XII); in acetic acid the process was complete in a few minutes. The yellow solution of the ester in aqueous sodium hydroxide probably contains a salt of the lactim modification; it becomes colourless if kept, and addition of acetic acid then precipitates only (XIII), whereas with the fresh solution it gives the initial ester.

The same methyl ester was obtained, together with much of (XII), when the corresponding silver salt was shaken in dry benzene with methyl iodide.

2-o-*Carbomethoxybenzoylphthalaz*-1 : 4-*dione* (XVI).—A mixture of *o*-carbomethoxybenzoyl chloride (5 g.) and phthalaz-1 : 4-dione (4 g.) in pyridine (30 c.c.) was left for 2 days, the pyridine hydrochloride and unchanged hydrazide removed, and the filtrate treated slowly with an excess of water. The crude *ester* was collected after 2 hours and purified from methyl alcohol or by solution in chloroform and addition of ether. It melted at 165—170° with decomposition and resolidification, melting again from 270—290°; a mixed m. p. with the methyl ester of (XIV) was depressed to 134—149° (Found: C, 63·1; H, 3·8. $C_{17}H_{12}O_5N_2$ requires C, 63·0; H, 3·7%). Thermal decomposition of the ester was complex, varying with the temperature. At 200—210° decomposition was rapid, but no methyl alcohol was produced; phthalic anhydride, (I), and a little of (XII) were isolated. But at 280°, methyl alcohol was evolved and a greater proportion of (XII) (0·14 g. from 0·45 g. of ester) was produced. The carbomethoxybenzoyl group can be removed from the phthalazine ring without complete hydrolysis of the carbomethoxy-group, for when the ester was refluxed with acetic acid for 2 hours, (I) was produced in the calculated quantity together with phthalic acid and methyl hydrogen phthalate. Aqueous alkali gave (I), phthalic acid, and methyl alcohol.

2 : 3-*Phthalophthalaz*-1 : 4-*dione* (XV).—Phthalaz-1 : 4-dione (5·7 g.) and *s*-phthalyl chloride (7·4 g.) were mixed with nitrobenzene (50 c.c.) and heated in an oil-bath at 160° with shaking. When the evolution of hydrogen chloride ceased (¾ hour), the temperature was raised to 210° for ¼ hour. The crystals which separated on cooling were usually free from (I); this, if present, was removed by solution in dilute aqueous ammonia. Crystallised from nitrobenzene, 2 : 3-*phthalophthalaz*-1 : 4-*dione* formed faintly yellow needles, m. p. 350—360° (slight decomp.) to a red liquid. It sublimed readily with little decomposition at 345—350°/15 mm. (Found: C, 65·7; H, 3·0; N, 9·9. $C_{16}H_8O_4N_2$ requires C, 65·7; H, 2·8; N, 9·6%). The yield was 9·4 g. (calc., 10·2 g.). The same condensation took place in pyridine at 100—110°, but the yield was smaller. (XV) was almost insoluble in the majority of organic solvents, but dissolved slightly in hot acetic acid, anisole, and amyl alcohol. Its solubility in nitrobenzene was 1 part in 35 (boiling) and 1 part in 500 (room temperature). Hydrazine, in aqueous or acetic acid solution, caused nearly quantitative conversion into (I). Boiling with 0·1N-sulphuric acid in acetic acid or with aqueous caustic soda brought about complete conversion into (I) and phthalic acid, and ammonium acetate in acetic acid gave (I) and phthalimide.

Condensation of Phthalyl Chlorides with Nitrophthalaz-1 : 4-*diones.*—6-Nitrophthalaz-

1 : 4-dione (2 g.) and *s*-phthalyl chloride (2·1 g.) in nitrobenzene (15 c.c.) were heated on an oil-bath at 190° for ½ hour (longer heating had no effect) in a stream of carbon dioxide. The solid dissolved, hydrogen chloride was evolved, and, on cooling, yellow crystals (3·3 g.) were obtained, m. p. 250—350°; extraction of these with hot anisole (25 c.c.) left pale yellow needles (0·75 g.), identified as (XV), m. p. 350—360°. The anisole extract gave an inseparable mixture of substances readily hydrolysed by cold aqueous ammonia.

A parallel result was obtained with 5-nitrophthalaz-1 : 4-dione. Substitution of pyridine for nitrobenzene caused no change in the nature of the products.

When 3-nitrophthalyl chloride (2·5 g.) and phthalaz-1 : 4-dione (2 g.) were condensed in nitrobenzene, a yield of 0·75 g. of (XV) was obtained.

1 : 4-*Dichlorophthalazine*.—Wolfram's method (D.R.-P. 481,650) was modified as follows: Phthalaz-1 : 4-dione (8 g.) and phosphorus pentachloride (25 g.) were heated on an oil-bath at 150° for 7 hours and the product was cooled, crushed, washed with petroleum, extracted (Soxhlet) with benzene, recovered from the extract, and crystallised from dry benzene; it formed long colourless needles (7 g.), m. p. 162—164°.

Condensation between phthalic acid and 1 : 4-dichlorophthalazine at 180° (alone or in nitrobenzene) gave chiefly 4-chlorophthalaz-1-one, m. p. 274°, insoluble in benzene, and phthalic anhydride. Pure 4-chlorophthalaz-1-one is colourless, and not yellow as stated by Radulescu.

Acetyl Derivatives of Phthalaz-1 : 4-dione.—Diacetyl derivative. Phthalaz-1 : 4-dione (3·2 g.) and acetic anhydride (20 c.c.) were refluxed together (½ hour to 24 hours); the crystals deposited on cooling were washed with dry ether; a further crop was obtained from the mother-liquor. 4-*Acetoxy-2-acetylphthalaz-1-one* formed colourless gable-ended needles from dry benzene; the m. p. was m. p. 139—140°, but invariably there was shrinkage from about 133° (Found: C, 58·6; H, 4·4; N, 11·6. $C_{12}H_{10}O_4N_2$ requires C, 58·55; H, 4·1; N, 11·4%). The substance was rapidly hydrolysed by aqueous alcohol, as found by Rowe and Peters.

Radulescu and Georgescu (*loc. cit.*) described a diacetyl derivative, m. p. 126°, obtained by using acetic anhydride and sodium acetate. Repetition of their experiment gave a crude product, m. p. 114—126°, but on purification this substance was found to be identical with the above diacetyl derivative, melting then at 137—140°.

Monoacetyl derivatives. (A) Phthalaz-1 : 4-dione (4·0 g.), acetyl chloride (2·4 g.), and pyridine (25 c.c.) were mixed at 0°, shaken in a freezing mixture, and then refluxed for 2 hours. After several days, crystals separated; they were washed with alcohol and ether and recrystallised from dry benzene, forming colourless needles (1·5 g.), which usually melted at 175—176°, but when placed in a bath at 165° and heated rapidly, melted at 180—183° (Found: C, 58·3; H, 4·2; N, 13·9. $C_{10}H_8O_3N_2$ requires C, 58·8; H, 4·0; N, 13·7%). Melting was accompanied by decomposition; a cloud of crystals always remained until near 200°. The *monoacetyl* derivative was completely converted into the preceding diacetyl derivative by refluxing with acetic anhydride. It was completely hydrolysed to (I) by boiling with 60% alcohol for 2 hours or by heating with dilute sodium hydroxide solution.

(B) 4-Acetoxy-2-acetylphthalazone (1 g.), absolute alcohol (0·3 c.c.), and benzene (5 c.c.) were refluxed on a water-bath for 3 hours and cooled; the crystals which had separated were extracted twice with boiling dry benzene. The residue, m. p. 165—170°, formed, after several recrystallisations from large volumes of dry benzene, flocks of white fibrous needles, electrified on rubbing, m. p. 172—173° (decomp.), a cloud of crystals remaining until 200°. The same product was obtained when the diacetyl derivative was boiled for a short time with 99% alcohol (Found: C, 58·6; H, 4·15; N, 14·2%). A mixture with the product obtained in (A) melted mostly at 160—165°, crystals remaining until 190°. Specimens of each of the pure materials, heated at the same time, were not molten at 172°.

(C) Phthalaz-1 : 4-dione was acetylated with acetic anhydride–acetic acid by the method of Rowe and Peters (*loc. cit.*). Repeated fractionation of the product from benzene gave a substance, m. p. 162—170°, but further fractionation from acetic acid yielded a product, m. p. 172—175° (a cloud of crystals remaining until 200°), and this was apparently a single substance. When it was mixed with the monoacetyl derivative obtained in (B), its m. p. was depressed to 160—170°. This substance was identical with the acetyl derivative obtained in (A).

Acethydrazide and Phthalic Anhydride.—Acethydrazide (1 g.) and phthalic anhydride (2 g.) were refluxed in acetic acid (10 c.c.) for ½ hour, cooled, and the crystalline product collected. After removal of small quantities of (XII) by boiling with benzene, *N*-acetamido-

phthalimide (2 g.) remained, m. p. 227—229° (Found: C, 58·45; H, 4·1%). The same condensation also took place at 140° in absence of a solvent.

Diacetylhydrazine and Phthalic Anhydride.—When diacetylhydrazine (3·5 g.) and phthalic anhydride (5 g.) were heated together at 140° for 15 hours, acetic acid distilled. The residue was extracted with boiling water and left 0·48 g. of (XII); the filtrate deposited *N*-acetamidophthalimide (2 g.), m. p. 228—230°.

Diacetylhydrazine (2·2 g.), phthalyl chloride (4 g.), and nitrobenzene (5 c.c.), when heated at 160° for 20 minutes, gave at first a clear solution, hydrogen chloride being evolved, and later deposited light yellow crystals (1·1 g.), identified as (XV).

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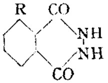
5. *Chemiluminescent Organic Compounds. Part II. The Effect of Substituents on the Closure of Phthalhydrazides to 5- and 6-Membered Rings.*

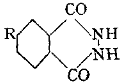
By H. D. K. Drew and F. H. Pearman.

The chemiluminescence of phthalaz-1 : 4-dione is modified on substitution of the phenyl group, but the effect is not predictable. Our objects were to investigate this point and revise the methods of preparation of phthalazdiones.

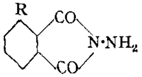
5-Nitrophthalaz-1 : 4-dione (I; R = NO_2) is best prepared from 3-nitrophthalic anhydride and just over 1 mol. of hydrazine in acetic acid, and *6-nitrophthalaz-1 : 4-dione* (II; R = NO_2) by the action of aqueous hydrazine (1 mol.) on 4-nitrophthalimide.



(I.)



(II.)



(III.)

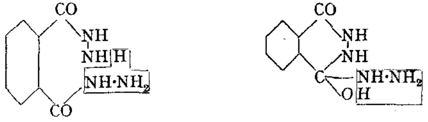
Reduction of 5- and 6-nitrophthalaz-1 : 4-diones to the more strongly luminescent amino-compounds (I and II; R = NH_2) gives impure products when ammonium sulphide or hydrazine is used as the reducing agent (compare Hoesch, *J. pr. Chem.*, 1907, **76**, 307; Radulescu and Alexa, *Bull. Soc. Chim. România*, 1930, **12**, 163; Huntress, *J. Amer. Chem. Soc.*, 1934, **56**, 241); but reduction with stannous chloride produces quantitative yields of colourless amines. The action of aqueous hydrazine on 3- or 4-aminophthalimide likewise gives the pure aminophthalazdione.

There is a significant distinction between the behaviour of 3-amino- and of 4-aminophthalimide with aqueous hydrazine: with 1 mol. of hydrazine the former gives *N : 3-diaminophthalimide* (III; R = NH_2) as practically the sole product, but with 2 mols. of hydrazine it gives only the 6-ring hydrazide (I; R = NH_2); whereas 4-aminophthalimide gives in either case only the 6-ring hydrazide (II; R = NH_2), the analogue of (III) not having been observed. Neither of these aminophthalimides reacts appreciably with hydrazine hydrate in glacial acetic acid, and reaction is slow in alcohol.

From this point of view, we have compared with these nitro- and amino-phthalimides the behaviour with hydrazine of four other substituted phthalimides. 3-Chlorophthalimide reacts with alcoholic hydrazine hydrate, giving *3-chloro-N-aminophthalimide* (III; R = Cl) with 1 mol. of hydrazine, but *5-chlorophthalaz-1 : 4-dione* (I; R = Cl) with 2 mols. of hydrazine; whereas *3-hydroxyphthalimide* reacts with aqueous hydrazine to give only *5-hydroxyphthalaz-1 : 4-dione* (I; R = OH), whether 1 mol. or 2 mols. of hydrazine are used. 3 : 6-Dichlorophthalimide, on the other hand, gives with either 1 mol. or 2 mols. of

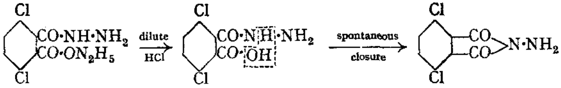
hydrazine hydrate in alcoholic solution only 3 : *6-dichloro*-N-*aminophthalimide*, and under similar conditions 4 : 5-dichlorophthalimide gives only 6 : *7-dichlorophthalaz*-1 : *4-dione*.

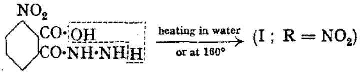
Further, a comparison was made of the behaviour of the substituted phthalic anhydrides with hydrazine. 3- and 4-Nitrophthalic anhydrides react with a slight excess over 1 mol. of hydrazine hydrate in acetic acid solution to give the 6-ring hydrazides as the end products. 3 : 6-Dichlorophthalic anhydride gives only 3 : 6-dichloro-*N*-aminophthalimide with 1 mol. of aqueous-alcoholic hydrazine, but with more than 2 mols. of hydrazine hydrate at 150° it gives only 5 : *8-dichlorophthalaz*-1 : *4-dione*; on the other hand, 4 : 5-dichlorophthalic anhydride reacts with 1 mol. of hydrazine hydrate in aqueous alcohol or in acetic acid to give 6 : 7-dichlorophthalaz-1 : 4-dione free from the 5-ring isomeride. It is notable that, parallel with these results, 3 : 6-dichlorophthalic acid forms its anhydride with unusual ease, whereas the 4 : 5-dichloro-acid does so reluctantly. So also 4 : 5-dichlorophthalimide is much less stable and more reactive than the 3 : 6-dichloro-isomeride. Tetrachlorophthalic acid or anhydride reacts with hydrazine hydrate at 150° to give only *tetrachloro*-N-*aminophthalimide* even when the hydrazine is in excess; the 6-ring hydrazide has not been prepared: the former compound has been mistaken for the latter by Phelps (*Amer. Chem. J.*, 1905, **33**, 586) and by Radulescu and Alexa (*loc. cit.*). A probable mechanism for the conversion of *N*-aminophthalimides into the corresponding phthalaz-1 : 4-diones by means of hydrazine is the opening of the phthalimide ring by addition of hydrazine, to form a dihydrazide, followed by closure in the new direction with extrusion of the added hydrazine; this can be regarded as a direct change (as shown below on the left) or as taking place through an intermediate 6-ring stage (on the right):



In other cases, where the presumed dihydrazides close to give *N*-aminophthalimides, analogous mechanisms are possible, the active hydrogen being here that of the imino- instead of the amino-group.

In two instances ring closure was observed of open-chain hydrazides whose structures were determined:

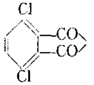
(1) 

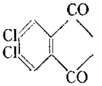
(2) 

These results, and others given in the experimental part, show that the type of ring-closure from open-chain compounds of this series, though it is not entirely unaffected by temperature, is mainly controlled by the nature of the substituents in the phenyl group, including those in the 1- and the 2-position. Thus, the other substituents being the same, the presence (in positions 1 : 2) of two $CO{\cdot}NH{\cdot}NH_2$ groups favours 6-ring formation, but that of one $CO{\cdot}NH{\cdot}NH_2$ and one $CO{\cdot}NH_2$ or CO_2H favours 5-ring formation; substitution of CO·NH·NHPh for one $CO{\cdot}NH{\cdot}NH_2$ also has the latter tendency. Again, where the 1 : 2 substituents remain unaltered, the nature and position of the other substituents pronouncedly influence the course of the closure. The latter effects may be summarised as follows: closure to the 5-ring is favoured by 3-Cl, 3-NH_2, 3 : 6-Cl_2, and 3 : 4 : 5 : 6-Cl_4 (Type *A*); whereas closure to the 6-ring is favoured by 3-OH, 4-NH_2, 4 : 5-Cl_2, and probably

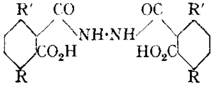
also by both 3-NO_2 and 4-NO_2 (*the effect of* 4-NO_2 *being the greater of the two*) (Type *B*).

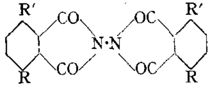
These effects may be accounted for by assuming that the positional substituents tend *to orient the Kekulé double bonds of the benzene ring* (compare Mills and Nixon, J., 1930, 2510). Then, the applicability of Baeyer's strain theory to rings containing both carbon and nitrogen being assumed, it is suggested (1) that the substituents of type *B*, which favour the 6-ring formation, tend to fix a double bond in the position common to the two rings, since in that case the 6-ring, whether or not it occurs in a lactim form, will have a smaller strain than the 5-ring; and (2) that those of type *A*, which favour the 5-ring formation, tend to fix the double bonds out of the common position, since in that case the 5-ring (which cannot assume a lactim form in the *N*-aminophthalimides) will have a smaller strain than the lactim form of the 6-ring:

(A.) 

 (B.)

s-*Bis*-(6-*nitro*-2-*carboxybenzoyl*)*hydrazine* (IV; R = H, R′ = NO_2) and s-*bis*-(3 : 6-*dichloro*-2-*carboxybenzoyl*)*hydrazine* (IV; R = R′ = Cl) have been prepared. Both compounds cyclise to the corresponding substituted *N*-phthalimidophthalimides (V),

(IV.) 

 (V.)

but from the nitro-compound a proportion of the phthalaz-1 : 4-dione also results. *Octachloro*-N-*phthalimidophthalimide*, which is free from hydrogen, also has been prepared.

Experimental.

3- and 4-Nitrophthalic acids were prepared by nitrating phthalic anhydride (500 g.) in presence of sulphuric acid ("Organic Syntheses," VII, 70); the mixture of the two acids was washed on sintered glass with concentrated hydrochloric acid (Blicke and Smith, *J. Amer. Chem. Soc.*, 1929, **51**, 1868) and crystallised twice from water and then from glacial acetic acid, the 3-nitro-acid being obtained in white hexagonal tablets (185 g.), m. p. 216—218°. The aqueous filtrates from the crystallisations were evaporated on the water-bath, and the residue dried at 100° (it chars above this temperature). A solution of the resulting crude 4-nitro-acid in absolute alcohol (600 c.c.) was saturated with hydrogen chloride and refluxed for 1 hour (Blicke and Smith, *loc. cit.*, give 12 hours; but compare Hayashi and Kawasaki, *J. Soc. Chem. Ind. Japan*, 1933, suppl. vol., 121), the 4-nitro-acid thus being converted into its ethyl ester, and the 3-nitro-acid into the 1-ethyl hydrogen ester (Kahn, *Ber.*, 1902, **35**, 3857), which is very resistant to further esterification (an appreciable quantity of the ethyl ester is formed if refluxing is prolonged). The mixture of esters was isolated and dissolved in ether, and the ethyl hydrogen ester removed by extraction with 10% aqueous sodium carbonate. The required ethyl 4-nitrophthalate distilled at 233—234°/38 mm. and solidified in flat needles, m. p. 34°; it was boiled with concentrated hydrochloric acid (500 c.c.) and water (500 c.c.) for 12 hours (Hayashi and Kawasaki, *loc. cit.*), and the 4-nitro-acid crystallised from 15% hydrochloric acid, forming colourless rhombs (205 g.), m. p. 164—166°.

Ethyl 4-*aminophthalate*, obtained by reduction of the 4-nitro-ester with zinc and aqueous-alcoholic hydrogen chloride, formed colourless needles, m. p. 97°.

3- and 4-Nitrophthalic anhydrides were obtained by heating the acids with acetic anhydride (2 mols.) for 10 minutes (see *op. cit.*, VII, 74). The 3-nitro-anhydride formed pale yellow needles, m. p. 163—164°, and was stable to moist air for a long time. The 4-nitro-anhydride formed white rods, m. p. 119—120°; it readily passed into the acid in moist air and was even partly hydrolysed on crystallisation from glacial acetic acid.

3- and 4-Nitrophthalimides were best prepared by heating an intimate mixture of the acid or its anhydride and ammonium carbonate ($1\frac{1}{4}$ mols.) at 220—230° with occasional stirring ($\frac{1}{2}$—1 hour); they were sufficiently pure for use. Crystallised from water, 3-nitrophthalimide

formed cream-coloured hexagonal plates, m. p. 216—217°, and the 4-nitro-isomeride cream-coloured square plates, m. p. 201—202°.

3- and 4-Aminophthalimides were prepared from the nitrophthalimides by reduction with stannous chloride and hydrochloric acid, as described by Levy and Stephen (J., **1931**, 79) for 4-aminophthalimide. Reduction of the 3-nitro-compound commenced only at 40°. The resulting hydrochlorides were hydrolysed to the aminophthalimides by repeated washing with boiling water. 3-Aminophthalimide formed bright yellow, feathery needles from water, m. p. 263—264° (decomp.), showing a green fluorescence in water or acetic acid and a violet in benzene as described by Kauffmann and Beisswenger (*Ber.*, 1903, **36**, 2494). Its 3-acetyl derivative (obtained by warming with acetic anhydride) melted at 242°, and its 3-*benzoyl* derivative (by means of benzoyl chloride in pyridine) formed cream-coloured silky needles, m. p. 249°, from acetic acid (Found: N, 10·6. $C_{15}H_{10}O_3N_2$ requires N, 10·5%); these derivatives were weakly fluorescent (violet) in water or acetic acid but not in benzene. 4-Aminophthalimide formed long, yellow, acicular needles from water, m. p. 294° (decomp.), and was not fluorescent; its acetyl derivative, likewise non-fluorescent, melted at 334°.

5-Nitrophthalaz-1 : 4-dione (I; R = NO_2) was best prepared by dissolving 3-nitrophthalic anhydride (96·5 g.) in boiling glacial acetic acid (400 c.c.), allowing the solution to cool for a few minutes, and then slowly stirring in hydrazine hydrate (26 g.; a slight excess over 1 mol.); the reaction was completed by ½ hour's boiling under reflux. The precipitate was removed (filtrate A), washed with hot acetic acid, and dissolved in 5% aqueous sodium hydroxide; the filtered solution gave pure 5-nitrophthalaz-1 : 4-dione (94—98 g.) when acidified with acetic acid.

Substitution of 3-nitrophthalic acid for the anhydride in the reaction gave a poor yield; but if, at the same time, alcohol was used as solvent, instead of acetic acid, acid hydrazine 3-nitrophthalate separated, and this, when heated alone at 150° in an air-stream (24 hours), gave 5-nitrophthalaz-1 : 4-dione in good yield (compare Bogert and Boroschek, *J. Amer. Chem. Soc.*, 1931, **53**, 745; Radulescu and Alexa, *Bull. Soc. Chim. România*, 1930, **12**, 140). This dione can also be prepared by heating 3-nitrophthalimide and aqueous hydrazine hydrate (1 mol. or 2 mols.) for 6 hours under reflux; much of it remains in the orange-red solution as a salt, but is precipitated by acetic acid (yield, nearly theoretical). When 3-nitrophthalimide is refluxed in alcoholic solution with hydrazine hydrate (1 mol.) for 1 hour, it is converted entirely into 5-nitrophthalaz-1 : 4-dione. This compound forms buff rhombic needles, m. p. 314° (decomp.), and is very sparingly soluble in water or acetic acid but more soluble in pyridine or nitrobenzene. There appear to be two isomeric monoacetyl derivatives. The first, prepared by heating the dione with acetic anhydride, has been described by Mihailescu and Protopopescu (*Bull. Soc. Chim. România*, 1930, **12**, 137), who give m. p. 230°; it was obtained as white fibrous needles, m. p. 221°, did not reduce Fehling's solution, and at once lost the acetyl group in presence of cold 5% sodium hydroxide solution. The second *monoacetyl* derivative was obtained from filtrate (A) above (particularly when the hydrazine was mixed first with the acetic acid) in buff hexagonal plates, m. p. 205° (Found: C, 48·4; H, 2·9; N, 16·8. $C_{10}H_7O_5N_3$ requires C, 48·2; H, 2·8; N, 16·9%), which reduced hot Fehling's solution and lost the acetyl group with 5% aqueous sodium hydroxide only on being boiled. The benzoyl derivative was obtained (by the use of benzoyl chloride and pyridine) in yellow needles, m. p. 228° (Mihailescu gives 200°); it was readily hydrolysed by cold 5% sodium hydroxide solution. 5-Nitrophthalaz-1 : 4-dione formed with hot 2*N*-aqueous ammonia lemon-yellow needles of an ammonium salt which was stable in air and could be recrystallised from water, and with hot 10% sodium carbonate solution orange hexagonal plates of a sodium salt.

3-*Nitro-2-carboxybenzhydrazide* was prepared from its 2-hydrazine salt (m. p. 157°), which was obtained by the method of Curtius and Semper (*Ber.*, 1913, **46**, 1162) from 1-ethyl hydrogen 3-nitrophthalate and hydrazine hydrate. The hydrazine salt was readily soluble in cold water, but when the solution was made just acid with dilute hydrochloric acid, white diamond-shaped needles of 3-nitro-2-carboxybenzhydrazide separated, m. p. 298—300° (decomp.) (Found: C, 42·9; H, 3·2. $C_8H_7O_5N_3$ requires C, 42·7; H, 3·1%). This substance reduced hot Fehling's solution, was only slightly soluble in water or alcohol, but soluble in alkalis, and when boiled with water for 2 hours or heated alone at 160° for 12 hours was converted into 5-nitrophthalaz-1 : 4-dione.

6-Nitrophthalaz-1 : 4-dione (II; R = NO_2) was best prepared from 4-nitrophthalimide (19·2 g.), suspended in water (125 c.c.), by adding hydrazine hydrate (5 g.; 1 mol.) in water (10 c.c.) and heating under reflux for 1 hour; most of it remained in the red solution as the ammonium salt and was precipitated by acetic acid (yield, 19·5 g.). It separated from 50%

acetic acid in small, pale yellow, hexagonal plates, m. p. 299—300° (decomp.), moderately easily soluble in water, alcohol, or pyridine. It was also prepared from the acid or anhydride as described for the 5-nitro-isomeride, than which it is more soluble, forms salts of deeper shade, and is more readily diacetylated; its ammonium salt forms orange needles.

5-Aminophthalaz-1 : 4-dione (I; R = NH_2).—(1) 3-Aminophthalimide (16·2 g.) was boiled with a solution of hydrazine hydrate (10 g.; 2 mols.) in water (100 c.c.) under reflux until evolution of ammonia ceased (1 hour); when the cooled solution was acidified with 10% acetic acid, the dione (17·7 g.) was precipitated. A solution of it in warm 5% aqueous sodium hydroxide was cooled to 0°, the sodium salt then crystallising in white hexagonal plates, easily decomposed by atmospheric carbon dioxide. The pure dione was precipitated from an aqueous solution of the sodium salt with dilute acetic acid.

(2) 5-Nitrophthalaz-1 : 4-dione (10 g.), dissolved in 5% aqueous sodium hydroxide (100 c.c.) at 50°, was added during 15 minutes to stannous chloride (45 g.) in concentrated hydrochloric acid (225 c.c.), with stirring, the temperature being kept at 50—60°. After cooling to 0°, 5-aminophthalaz-1 : 4-dione hydrochloride separated in needles; this was collected, washed, and freed from any tin salts by extraction in aqueous ammonia (10%) and filtration. Acidification of the filtrate with dilute acetic acid gave pure 5-aminophthalaz-1 : 4-dione (6·5 g.). A further amount was obtained from the filtrate by making it alkaline with sodium hydroxide, acidifying the solution with acetic acid, and purifying the precipitate as before (total yield, nearly theoretical).

5-Aminophthalaz-1 : 4-dione is a white crystalline powder, m. p. 332—333° (decomp.), very sparingly soluble in the usual solvents; its solutions in water, acetic acid, dilute hydrochloric acid, alcohol, and acetone show a violet fluorescence, but not solutions in benzene, alkalis, or strong mineral acids. It dissolves in alkalis, forming salts decomposed by carbon dioxide, and in strong mineral acids, giving salts hydrolysed by hot water. The ammonium salt separates in colourless rods, hydrolysed by boiling water, and the hydrochloride in colourless needles, which lose hydrogen chloride when heated. The barium salt forms long cream-coloured needles. With acetic anhydride the amino-dione gives long white needles of 5-acetamidoacetylphthalaz-1 : 4-dione, m. p. 262° (from dry benzene) (Found: C, 55·3; H, 4·4; N, 16·3. Calc. for $C_{12}H_{11}O_4N_3$: C, 55·2; H, 4·2; N, 16·1%). When this substance is dissolved in dilute aqueous ammonia (10 mins.' boiling), and the solution acidified with acetic acid, white micro-crystals of *5-acetamidophthalaz-1 : 4-dione* (I; R = NH·CO·CH_3), m. p. 325—326° (decomp.), separate (Found: N, 19·1, 19·25. $C_{10}H_9O_3N_3$ requires N, 19·2%), which forms a sodium salt with 5% aqueous sodium hydroxide. Its solutions are not fluorescent. The same substance was obtained by the action of (*a*) hydrazine hydrate (1 mol.) on 3-acetamidophthalimide in boiling alcohol and (*b*) hydrazine hydrate on 3-acetamidophthalic anhydride (Lawrence, *J. Amer. Chem. Soc.*, 1920, **42**, 1872). *5-Benzamidophthalaz-1 : 4-dione* (I; R = NH·COPh) was obtained, by the action of an excess of alcoholic or aqueous hydrazine hydrate on 3-benzamidophthalimide, in small white needles (from nitrobenzene), m. p. 319° (decomp.) (Found: C, 64·1; H, 3·8; N, 14·9. $C_{15}H_{11}O_3N_3$ requires C, 64·1; H, 3·5; N, 14·9%). Treatment of the sodium salt of 5-aminophthalaz-1 : 4-dione in pyridine with benzoyl chloride gave silver-white hexagonal plates, m. p. 263°, of the *dibenzoyl* derivative (Found: C, 68·8; H, 4·0. $C_{22}H_{15}O_4N_3$ requires C, 68·6; H, 3·9%).

N : *3-Diaminophthalimide* (III; R = NH_2) was practically the sole product when 3-aminophthalimide was treated with hydrazine (1 mol.) in water as in the preparation of the 5-amino-dione (above). It crystallised from water in bright yellow, rhombic needles (Found: C, 54·4; H, 4·0. $C_8H_7O_2N_3$ requires C, 54·2; H, 3·95%), which melted at 252° and resolidified as 5-aminophthalaz-1 : 4-dione. The last compound is the by-product of the preparation and is removed by washing with cold 2% sodium hydroxide solution, in which *N* : 3-diaminophthalimide is insoluble. The latter is also much more readily soluble in water, alcohol, or acetic acid, and reduces hot Fehling's solution. It is converted into the sodium or hydrazine salt of the amino-dione by boiling (½ hour) with 5% aqueous sodium hydroxide or aqueous hydrazine hydrate (1 mol.), open-chain compounds being produced as intermediates.

*3-Acetamido-*N*-anilinophthalimide* was prepared by condensing 3-acetamidophthalic anhydride and phenylhydrazine in acetic acid solution; it formed pale buff needles, m. p. 179° (Found: N, 14·3. $C_{16}H_{13}O_3N_3$ requires N, 14·2%), insoluble in dilute alkali solution.

6-Aminophthalaz-1 : 4-dione (II; R = NH_2).—This could only be obtained satisfactorily (1) by the action of 1 mol. of hydrazine hydrate (5 g. in 200 c.c. of water) on 4-aminophthalimide (16·2 g.), the sodium salt being isolated in colourless needles, and (2) by reduction of 6-nitrophthalaz-1 : 4-dione, both methods being those described for the preparation of the 5-amino-

compound. It forms small colourless needles, m. p. 339° (decomp.), and is more soluble than the 5-amino-isomeride; it is also less basic, showing little tendency to form salts with mineral acids. Its solutions are not fluorescent.

6-Acetamidophthalaz-1 : 4-*dione* (II; R = NH·CO·CH_3), prepared by refluxing 4-acetamidophthalimide with hydrazine hydrate, formed small white prisms from water, m. p. 341° (decomp.) (Found: N, 19·3. $C_{10}H_9O_3N_3$ requires N, 19·2%). It forms a sodium salt with 5% sodium hydroxide solution.

3-*Nitro*-N-*anilinophthalimide*.—3-Nitrophthalic anhydride (3·8 g.) in glacial acetic acid (10 c.c.) was mixed with a saturated aqueous solution of phenylhydrazine hydrochloride (2·2 g.) and sodium acetate (3 g.) and refluxed for ½ hour. The precipitate was washed with water and with 2% sodium hydroxide solution and crystallised from glacial acetic acid, forming pale yellowish-brown plates, m. p. 188° (Found: N, 14·7. $C_{14}H_9O_4N_3$ requires N, 14·8%), only slightly soluble in water and insoluble in cold alkali. A small proportion of the dione also was produced.

s-*Bis*-(6-*nitro*-2-*carboxybenzoyl*)*hydrazine* (IV; R = H, R′ = NO_2. The orientation of the carboxyl groups, though probable, has not been proved).—Powdered 3-nitrophthalic anhydride (2·8 g.) was suspended in glacial acetic acid (20 c.c.), and hydrazine hydrate (0·7 g.; 1 mol.) in acetic acid (20 c.c.) rapidly added with stirring. The mixture of the required *substance* and its hydrazine salt deposited from the colourless solution after 1 hour was collected and dissolved in just sufficient cold 5% aqueous sodium hydroxide; when the solution was acidified with dilute hydrochloric acid, long cream-coloured needles, m. p. about 318° (decomp.) (depending on the rate of heating), separated (Found: C, 46·0; H, 2·7; N, 13·3. $C_{16}H_{10}O_{10}N_4$ requires C, 45·9; H, 2·4; N, 13·4%). Recrystallisation was impossible. The substance formed an acid solution in water and reduced Fehling's solution.

3-*Chloro*-N-*aminophthalimide* (III; R = Cl).—3-Chlorophthalimide (m. p. 236°; prepared from diazotised 3-aminophthalimide by the Sandmeyer process) was refluxed for 1 hour with hydrazine hydrate (1 mol.) in alcohol (96%), ammonia being evolved. The *product* was washed with dilute aqueous ammonia and recrystallised from water, forming cream-coloured needles, m. p. 194—195° (Found: C, 48·6; H, 2·7. $C_8H_5O_2N_2Cl$ requires C, 48·8; H, 2·5%). It reduced Fehling's solution and was insoluble in cold 5% sodium hydroxide solution. In the above reaction only a little of the following compound was produced.

5-*Chlorophthalaz*-1 : 4-*dione* (I; R = Cl).—(*a*) A mixture of 3-chlorophthalimide and hydrazine hydrate (2 mols.) in alcohol (96%) was refluxed for 1 hour, and the resulting yellow solution acidified with dilute acetic acid. (*b*) 5-Aminophthalaz-1 : 4-dione (2 g.), dissolved in concentrated sulphuric acid (12 c.c.), was treated at 0° with sodium nitrite (1 g.) in concentrated sulphuric acid (10 c.c.), with vigorous stirring; phosphoric acid (60 c.c.; *d* 1·7) at 0° was then slowly added (see Schoutissen, *J. Amer. Chem. Soc.*, 1933, **55**, 4531). After 1 hour at 0° the mixture was treated with urea (2 g.), poured on ice, rapidly run into a solution of cuprous chloride (from 2 g. of copper sulphate) in hydrochloric acid, stirred for 1 hour, and then heated on a water-bath. The precipitate was removed, dissolved in dilute sodium hydroxide solution, and reprecipitated with acetic acid.

5-*Chlorophthalaz*-1 : 4-*dione* formed cream-coloured micro-needles, m. p. 338° (decomp.) from nitrobenzene or much water (Found: C, 48·7; H, 2·7; N, 14·3. $C_8H_5O_2N_2Cl$ requires C, 48·8; H, 2·5; N, 14·2%). It did not reduce Fehling's solution and was completely soluble in dilute aqueous alkali. The above diazo-solution coupled with alkaline β-naphthol, giving scarlet needles (from alcohol) of the *azo-compound* (Found: N, 17·1. $C_{18}H_{12}O_3N_4$ requires N, 16·9%).

3 : 6-*Dichloro*-N-*aminophthalimide*.—(1) Hydrazine hydrate (5 g.; 1 mol.) in water (10 c.c.) was added to a solution of 3 : 6-dichlorophthalic anhydride (21·5 g.) (ethyl hydrogen 3 : 6-dichlorophthalate can be used) in hot 96% alcohol (50 c.c.) and heated under reflux (1 hour); needles (15 g.; 5 g. more can be obtained from the filtrate) separated on cooling, and addition of water (120 c.c.). (2) 3 : 6-Dichlorophthalimide and hydrazine hydrate (1 mol.) were refluxed (1 hour) in alcohol, and water added. When 2 mols. of hydrazine hydrate were used in the latter reaction, the hydrazine salt of the acid hydrazide, and not the dione, was produced.

3 : 6-*Dichloro*-N-*aminophthalimide* crystallised from water in almost white, flat needles (Found: C, 41·7; H, 1·8; N, 12·3. $C_8H_4O_2N_2Cl_2$ requires C, 41·6; H, 1·7; N, 12·1%); it melted at 210°, resolidified in a few minutes, and did not melt again below 350°. It was soluble in water (solution neutral), alcohol, or acetic acid (hot solutions are deep yellow), but insoluble in cold alkalis, although it dissolved on warming. In alcoholic solution it at once reacted with hydrazine hydrate to give acicular needles of the *hydrazine* salt of 3 : 6-dichloro-2-carboxy-

benzhydrazide (Found for a sample dried over phosphoric oxide: C, 34·2; H, 3·5. $C_8H_4O_3N_2Cl_2,N_2H_4$ requires C, 34·2; H, 3·5%), which on dehydration gave 3 : 6-*dichlorophthalodihydrazide* (Found for the substance dehydrated at 100°: C, 36·7; H, 3·1; N, 21·3. $C_8H_8O_2N_4Cl_2$ requires C, 36·5; H, 3·0; N, 21·3%). The former substance (hydrazine salt) reduced Fehling's solution in the cold. It dissolved in cold water and the solution soon deposited 3 : 6-dichloro-*N*-aminophthalimide; boiling water or a drop of dilute hydrochloric acid effected the change at once. 3 : 6-Dichloro-*N*-aminophthalimide reduced warm Fehling's solution, formed a *benzylidene* derivative in aqueous alcoholic solution (10 mins.' boiling), consisting of blunt needles, m. p. 224° (Found: N, 8·9. $C_{15}H_8O_2N_2Cl_2$ requires N, 8·8%), and was converted by sodium nitrite in warm acetic acid solution into 3 : 6-dichlorophthalimide and by 3 : 6-dichlorophthalic anhydride in acetic acid (5 mins.' boiling) into 3 : 6 : 3′ : 6′-tetrachloro-*N*-phthalimidophthalimide.

3 : 6 : 3′ : 6′-*Tetrachloro*-N-*phthalimidophthalimide* (V; R = R′ = Cl) separated in white needles (2 g.) when 3 : 6-dichlorophthalic anhydride (2·1 g.) and hydrazine hydrate (0·25 g.; ½ mol.) were refluxed in glacial acetic acid (20 c.c.) for ½ hour; and was also formed when 3 : 6-dichloro-*N*-aminophthalimide was kept at its m. p. for ½ hour, hydrazine being evolved. It crystallised from nitrobenzene in diamond-shaped crystals, m. p. above 350° (Found: C, 44·8; H, 1·2; N, 6·6. $C_{16}H_4O_4N_2Cl_4$ requires C, 44·6; H, 0·9; N, 6·5%). It was insoluble in water, acetic acid, or cold alkali, but hot 5% sodium hydroxide solution hydrolysed it to 3 : 6-dichloro-*N*-aminophthalimide and 3 : 6-dichlorophthalic acid.

5 : 8-*Dichlorophthalaz*-1 : 4-*dione*.—When 3 : 6-dichlorophthalic anhydride (4 g.) was mixed with hydrazine hydrate (3 g.; more than 3 mols.), heat was evolved and the anhydride dissolved. After 1 hour's heating at 120—130° the residue was dissolved in warm 2½% aqueous sodium hydroxide, and the filtered solution acidified with dilute acetic acid; this process was repeated. The *dione* (3·6 g.) formed small cream-white needles from nitrobenzene, m. p. above 350° (Found: C, 41·6; H, 1·9; N, 12·0. $C_8H_4O_2N_2Cl_2$ requires C, 41·6; H, 1·7; N, 12·1%), and had the expected properties. Its sodium salt (cream-coloured rhombic plates) and ammonium salt (needles) were sparingly soluble and their aqueous solutions were yellow. The dione was also formed when (1) hydrazine 3 : 6-dichlorophthalate was heated at 165° for 6 hours, and (2) 3 : 6-dichloro-*N*-aminophthalimide was heated with hydrazine hydrate (1 mol.) at 160°, or with hydrazine hydrate (2 mols.) at 120—130°, for 1 hour.

s-*Bis*-(3 : 6-*dichloro*-2-*carboxybenzoyl*)*hydrazine* (IV; R = R′ = Cl).—3 : 6-Dichlorophthalic anhydride (2·1 g.) was suspended in glacial acetic acid (20 c.c.), and hydrazine hydrate (0·5 g.) in acetic acid (20 c.c.) rapidly added with stirring. The precipitated hydrazine salt was collected after 1 hour and dissolved in water, and the *acid* precipitated by means of dilute hydrochloric acid in colourless needles, m. p. above 350° (Found: C, 41·4; H, 1·6. $C_{16}H_8O_6N_2Cl_4$ requires C, 41·2; H, 1·7%). It reduced hot Fehling's solution and was at once soluble in dilute alkali solution. It was only slightly soluble in the ordinary solvents and could not be recrystallised without decomposition. Boiling with glacial acetic acid caused ring closure to 3 : 6 : 3′ : 6′-tetrachloro-*N*-phthalimidophthalimide.

Hydrazine 3 : 6-*dichlorophthalate* was obtained, from hydrazine and the acid in alcohol, in colourless hexagonal plates, m. p. 206° (resolidification), soluble in cold water (Found: C, 31·9; H, 4·2. $C_8H_4O_4Cl_2,2N_2H_4$ requires C, 32·1; H, 4·0%).

6 : 7-*Dichlorophthalaz*-1 : 4-*dione*.—(1) A solution of 4 : 5-dichlorophthalic anhydride (21·5 g.) in glacial acetic acid (120 c.c.) was refluxed with hydrazine hydrate (5 g.; more than 1 mol.) for ½ hour (yield, 19·8 g.). The reaction proceeds in the same manner in aqueous alcohol. (2) An alcoholic solution of 4 : 5-dichlorophthalimide containing hydrazine hydrate (1 mol.) was boiled for a few minutes. The *product* was completely soluble in alkali, giving yellow solutions. It formed white diamond-shaped prisms, m. p. above 350° (Found: C, 41·5; H, 1·8. $C_8H_4O_2N_2Cl_2$ requires C, 41·6; H, 1·7%), insoluble in the ordinary solvents. The sodium and the ammonium salt formed cream-coloured needles and were sparingly soluble in water.

3 : 4 : 5 : 6-*Tetrachloro*-N-*aminophthalimide*.—(1) Tetrachlorophthalic acid in alcoholic solution was treated with hydrazine hydrate (1 mol.) and the white precipitate which separated was heated on an oil-bath for 12 hours at 140—150°; the yellow residue was powdered, extracted with warm water, and crystallised from glacial acetic acid (compare Radulescu and Alexa, *loc. cit.*). (2) Tetrachlorophthalic anhydride (5 g.) was dissolved in alcohol (25 c.c.) and mixed with hydrazine hydrate (0·9 g.; 1 mol.) in water (25 c.c.); the mixture was refluxed for 1 hour. The colourless plates (4·5 g.) which separated were washed with water and crystallised from glacial acetic acid. *Tetrachloro*-N-*aminophthalimide* formed colourless, flat, rhombic needles, m. p. 288° (decomp.) (Found: N, 9·3. $C_8H_2O_2N_2Cl_4$ requires N, 9·3%), almost insoluble in water

or alcohol. It gave deep yellow solutions in glacial acetic acid or nitrobenzene. It was insoluble in cold aqueous caustic alkali or carbonate, but slowly dissolved in hot alkali and slowly separated when the solution was made acid. In hot acetic acid it was converted into tetrachlorophthalimide, m. p. 335°, by sodium nitrite. It reduced hot Fehling's solution. When boiled for 5 minutes with benzaldehyde in acetic acid it gave a *benzylidene* derivative, which formed pale yellow plates from alcohol, m. p. 232° (Found: N, 7·4. $C_{15}H_6O_2N_2Cl_4$ requires N, 7·2%).

Octachloro-N-*phthalimidophthalimide* (as V) was obtained by heating tetrachlorophthalic anhydride with 3 : 4 : 5 : 6-tetrachloro-*N*-aminophthalimide in glacial acetic acid for 10 minutes; the deep yellow colour of the solution disappeared, and long, white, acicular needles, m. p. above 350°, separated on cooling (Found: N, 4·9. $C_{16}O_4N_2Cl_8$ requires N, 4·9%).

3-*Hydroxyphthalimide*.—The use of hydrochloric acid in the following diazotisation leads to contamination of the product with 3-chlorophthalimide. 3-Aminophthalimide (4·8 g.) was dissolved in concentrated sulphuric acid (10 c.c.) at room temperature, cooled, and diluted to 30 c.c. with dry ice. The suspension of sulphate formed was diazotised at 0·5° with sodium nitrite (2·2 g. in 5 c.c. of water); the filtered diazo-solution (orange) was decomposed on the water-bath (2 hours), and the buff precipitate dried, sublimed at its m. p., and crystallised from water, yielding 3-*hydroxyphthalimide* in colourless needles (2·9 g.), m. p. 255—256°, soluble in cold alkali to a deep yellow solution with a strong green fluorescence, from which it was reprecipitated by acetic acid. It was soluble also in hot water or alcohol to green fluorescent solutions, and gave a deep red colour with ferric chloride (Found: C, 59·3; H, 3·2. $C_8H_5O_3N$ requires C, 59·0; H, 3·1%).

5-*Hydroxyphthalaz*-1 : 4-*dione* (I; R = OH).—This could not be obtained free from coloured impurities when prepared by diazotisation of 5-aminophthalaz-1 : 4-dione, but was obtained pure as follows. 3-Hydroxyphthalimide (1·6 g.) and hydrazine hydrate (1·0 g.; 2 mols.) were refluxed together for 1 hour, in water (20 c.c.); the pale yellow solution was then made acid with dilute acetic acid, and the white precipitate crystallised from a large volume of hot water. The *hydroxy-dione* formed white hexagonal rods, m. p. 330° (decomp.), readily soluble in alkalis to colourless solutions. It gave a deep brown coloration with ferric chloride (Found: C, 54·0; H, 3·6. $C_8H_6O_3N_2$ requires C, 53·9; H, 3·4%). The *mono-sodium* salt was prepared in long white needles (Found: Na, 11·2. $C_8H_5O_3N_2Na$ requires Na, 11·5%).

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6. *Chemiluminescent Organic Compounds. Part III.* N-*Methylated Phthalaz*-1 : 4-*diones*.*

By H. D. K. DREW, H. H. HATT, and F. A. HOBART.

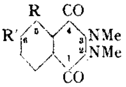
PHTHALAZ-1 : 4-DIONES show luminescence only when oxidised in solutions containing alkali, and therefore preliminary enolisation (lactim formation) has been assumed to occur. We wished to examine this hypothesis by finding what effect on the luminescence, particularly of the highly luminescent amino-derivatives, took place when one or both of the enolisable hydrogen atoms were replaced by the immobile methyl group. Direct methylation of the diones might give methylated lactim or lactam forms or a mixture of both; and therefore the methylated compounds were prepared by acting upon phthalic anhydrides and phthalimides with methylated hydrazines, whereby only *N*-methyl derivatives can result.

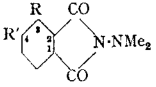
Rowe and Peters (J., 1933, 1331) prepared 2-methylphthalaz-1 : 4-dione from phthalic anhydride and methylhydrazine in acetic acid. We have not been able to prepare the 5-ring isomeride, *N*-methylaminophthalimide, either by modifying this reaction or by the action of methylhydrazine on phthalimide. It appears, therefore, that 6-ring formation is

* Since the completion of this paper a memoir by Zellner and Dougherty (*J. Amer. Chem. Soc.*, 1936, 58, 1811) has appeared which covers common ground. Their descriptions of substances differ markedly from ours in a number of instances.

enhanced by the presence of the methyl group in the open-chain intermediate compounds (compare the case of hydrazine, Part I, this vol., p. 16); this conclusion receives some support from the fact that only the diones were isolated (see below) on condensing methylhydrazine with 3- or with 4-nitrophthalic anhydride.

Condensation of phthalic anhydride with *s*-dimethylhydrazine gave the colourless 2 : 3-*dimethylphthalaz*-1 : 4-*dione* (I; R = R′ = H), as would be expected, and with *as*-dimethylhydrazine the more fusible, pale yellow isomeride, *N*-dimethylaminophthalimide


(I.)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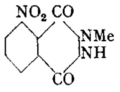
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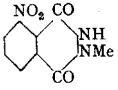
(IV.)

(II; R = R′ = H). In a similar way, 5- and 6-*nitro*-2 : 3-*dimethylphthalaz*-1 : 4-*diones* and 3- and 4-*nitro*-N-*dimethylaminophthalimides* were obtained from 3- and 4-nitrophthalic anhydrides. By reduction of the nitro-compounds, 5- and 6-*amino*-2 : 3-*dimethylphthalaz*-1 : 4-*diones* were obtained.

As was to be anticipated, the action of methylhydrazine on 3-nitrophthalic anhydride gave a mixture separable into two isomerides, α- and β-5-*nitro*-N-*methylphthalaz*-1 : 4-*diones*, which behave as typical diones and so must comprise structures (III) and (IV); they are pale yellow substances forming colourless *acetyl* derivatives. The α-compounds are the less fusible and soluble, but it has not yet been ascertained whether they have the methyl group in the 2- or the 3-position. These nitro-compounds were reduced to the desired α- and β-5-*amino*-N-*methylphthalaz*-1 : 4-*diones*, the α- being the less fusible.

Parallel results were obtained in the condensation of 4-nitrophthalic anhydride with methylhydrazine; of the α- and β-6-*nitro*-N-*methylphthalaz*-1 : 4-*diones*, which are fairly readily separable, the α-form is the less soluble and fusible, and the same applies to the *acetyl* derivatives, but on the other hand β-6-*amino*-N-*methylphthalaz*-1 : 4-*dione* is less soluble and fusible than its *α-isomeride*.

A monomethyl derivative (m. p. 264°) of 5-nitrophthalaz-1 : 4-dione was obtained by Mihailescu and Protopopescu (*Bul. Soc. Chim. România*, 1930, **12**, 95) by the action of methyl sulphate; and a similar 6-nitro-compound (m. p. 298°) was prepared by Hoesch and Curtius (*J. pr. Chem.*, 1907, **76**, 301), using the same method. The descriptions are not sufficient to show whether these substances are identical with any of the four isomerides now described.

The 5-ring compounds and the dimethylated diones here described were devoid of luminescence; so also were the monomethylated 5- and 6-nitro-diones, but, of the four amino-derivatives prepared from them, three showed distinct though very feeble luminescence. The α-6-amino-compound did not glow on oxidation; of the remainder, the β-5-amino-compound was the most luminescent. The glows exhibited by these substances were all exceedingly feeble compared with that of the unmethylated 5-amino-dione, and therefore we cannot yet conclude that their luminescence is intrinsic and not the result of impurity;* further work is being carried out on the point. The present conclusion, therefore, is that the substitution of immobile groups for two of the enolisable hydrogen atoms of phthalaz-1 : 4-diones removes the luminescence, and that the substitution even for one of them very greatly diminishes, if it does not entirely remove, that property.

Experimental.

2-Methylphthalaz-1 : 4-dione, prepared by the method of Rowe and Peters (*loc. cit.*), formed colourless rhombic crystals (from glacial acetic acid), m. p. 238°. It also resulted in attempts to prepare *N*-methylaminophthalimide by the condensation of phthalimide and methylhydrazine under various conditions.

2 : 3-*Dimethylphthalaz*-1 : 4-*dione*.—Phthalic anhydride (5 g.), *s*-dimethylhydrazine dihydro-

* The presence of traces of hydrazine in the methyl- and dimethyl-hydrazine used would give rise to 5- and 6-aminophthalaz-1 : 4-diones, both of which are luminescent.

chloride (4·9 g.), and hydrated sodium acetate (10 g.) were refluxed together (3 hours) in 50% aqueous acetic acid; the acetic acid was then removed by repeated vacuum distillation with water. The residue crystallised from water in long, colourless, efflorescent needles of the *dihydrate* (Found, by detailed observation of the rate of loss of water at 20°: H_2O, 15·9. $C_{10}H_{10}O_2N_2,2H_2O$ requires H_2O, 15·95%). The *anhydrous* substance, m. p. 175—176°, was white [Found: C, 63·3; H, 5·6; N, 14·7; *M* (in camphor), 188. $C_{10}H_{10}O_2N_2$ requires C, 63·15; H, 5·25; N, 14·75%; *M*, 190]. Hydrolysis by hot 2*N*-hydrochloric acid (3 hours) gave phthalic acid and dimethylhydrazine; boiling aqueous hydrazine gave the latter and phthalaz-1 : 4-dione.

N-*Dimethylaminophthalimide*.—Phthalic anhydride (2·4 g.) and *as*-dimethylhydrazine (1·0 g.) were heated together on the water-bath (2 hours); the oily red-brown product was boiled with water, the solution, on cooling, giving the required *substance* (1·4 g.), which crystallised from water (charcoal) in pale yellow plates, m. p. 125—126° [Found: C, 63·25; H, 5·35; *M* (in camphor), 185. $C_{10}H_{10}O_2N_2$ requires C, 63·15; H, 5·25%; *M*, 190], very soluble in alcohol or acetic acid. *N*-Hydrochloric acid hydrolysed it readily, producing phthalic acid, and treatment with hydrazine gave phthalaz-1 : 4-dione. The above condensation proceeded less favourably in acetic acid as solvent.

α- *and* β-5-*Nitro*-N-*methylphthalaz*-1 : 4-*diones*.—3-Nitrophthalic anhydride (2 g.), dissolved in glacial acetic acid (12 c.c.), was mixed slowly with methylhydrazine (1 g.), and the solution gently boiled under reflux (2 hours). The mixture, m. p. 235—245°, of two isomerides (1·9 g.) obtained on standing was separated either by taking advantage of the supersaturation of the β-isomeride in glacial acetic acid, or by acetylating the mixture (acetic anhydride) and fractionally crystallising the product from acetic acid; the pure α-acetyl derivative separated first and long needles of the β-acetyl derivative were slowly deposited from the mother-liquor after dilution with water. The acetyl derivatives were easily converted into the required nitro-compounds by shaking with dilute sodium hydroxide solution and precipitation with acid. The separations were followed by observing the m. p.'s and mixed m. p.'s of the several fractions. The α-*nitro*-compound formed very pale yellow, rhombic plates, m. p. 292° (decomp.) (Found: C, 49·1; H, 3·0; N, 19·6. $C_9H_7O_4N_3$ requires C, 48·85; H, 3·15; N, 19·0%), its sodium salt orange needles, and its *acetyl* derivative colourless rectangular or hexagonal prisms (from acetic acid) or long colourless needles (from alcohol), m. p. 204—205° (Found: C, 50·25; H, 3·4. $C_{11}H_9O_5N_3$ requires C, 50·2; H, 3·4%). The β-*nitro*-compound formed very pale yellow, pointed plates, m. p. 272° (decomp.) (Found: C, 49·15, 48·95; H, 3·35, 3·8; N, 19·3%); its *acetyl* derivative formed long, thin, colourless, pointed needles of tough texture, m. p. 158° (Found: C, 50·2; H, 3·7%); it is very triboelectric. Mixtures of the α- and the β-nitro-compound show a large depression of m. p.; and the same is true of their acetyl derivatives.

α- *and* β-5-*Amino*-N-*methylphthalaz*-1 : 4-*diones*.—These amines were obtained by reducing the above nitro-compounds with tin and concentrated hydrochloric acid at 30—40° with shaking. If they did not separate as stannichlorides from the filtered liquor, the whole was diluted with water and neutralised with excess of chalk, the mixture boiled and filtered, and the filtrate cautiously neutralised with dilute hydrochloric acid; the amine separated on standing. Tin can also be removed by hydrogen sulphide from solutions made just acid with acetic acid. The α-*amine* formed cream-coloured hexagonal columns from acetic acid, m. p. 308° (decomp.; sintering above 300°); dilute solutions had a blue fluorescence when cold (Found: C, 56·4; H, 5·0. $C_9H_9O_2N_3$ requires C, 56·55; H, 4·7%). The β-*amine* formed pale cream-coloured, long, thin needles from water, in which it was appreciably soluble; it melted at 299° (decomp.; superficial darkening from 240°) and depressed the m. p. of the α-isomeride; its solutions had a strong blue fluorescence (Found: C, 56·35; H, 5·2%). These amines dissolved at once in aqueous ammonia to colourless solutions; they were also soluble in mineral acids, to solutions which could be diazotised and coupled with alkaline β-naphthol, giving red alkali-soluble *azo*-compounds.

5-*Nitro*-2 : 3-*dimethylphthalaz*-1 : 4-*dione*.—A mixture of 3-nitrophthalic anhydride (7 g.), *s*-dimethylhydrazine hydrochloride (6 g.), anhydrous sodium acetate (6 g.), and acetic acid (35 c.c.) was heated under reflux (3 hours); the acetic acid was removed by repeated evaporation with water, and the residue washed with water, being then almost pure (6·8 g.). The *substance* crystallised from water in pale canary-yellow, anhydrous, rhombic platelets, m. p. 194—195° [Found: C, 50·95; H, 4·05; N, 18·3; *M* (in camphor), 241. $C_{10}H_9O_4N_3$ requires C, 51·05; H, 3·85; N, 17·85%; *M*, 235], very soluble in acetic acid but rather sparingly soluble in water or alcohol. Hydrolysis to *s*-dimethylhydrazine by hot 2*N*-hydrochloric acid required about 16 hours.

3-*Nitro*-N-*dimethylaminophthalimide*.—3-Nitrophthalic anhydride (3·1 g.) and *as*-dimethyl-

hydrazine (1 g.) were separately dissolved in a little acetic acid, and the solutions mixed; the acetic acid was then evaporated, the residue heated at 100° for ½ hour, at 180° for 1 minute, cooled, and rubbed with water, and the remaining solid crystallised from toluene and from alcohol. The *compound* formed pale yellow leaflets, m. p. 141—142° [Found: C, 51·45; H, 4·0; N, 18·2; *M* (in camphor), 240. $C_{10}H_9O_4N_3$ requires C, 51·05; H, 3·85; N, 17·85%; *M*, 235]. Mineral acid readily hydrolysed it to 3-nitrophthalic acid; it was not very soluble in boiling water but after some time went into solution as dimethylhydrazine 3-nitrophthalate, which was isolated in colourless needles.

5-*Amino*-2 : 3-*dimethylphthalaz*-1 : 4-*dione*.—This, prepared from the corresponding nitro-compound by reduction with stannous chloride and concentrated hydrochloric acid at about 50°, separated as the stannichloride, which was decomposed with chalk and water, as described above. The *amine* (yield, 80%) crystallised from water in anhydrous, very pale yellow, hexagonal prisms, or rhombic needles, m. p. 192° (Found: C, 58·9; H, 5·6. $C_{10}H_{11}O_2N_3$ requires C, 58·5; H, 5·4%), soluble in hot water (1 in 10) or alcohol and very soluble in hot acetic acid; there was some evidence that it formed an unstable hydrate. Its *acetyl* derivative formed white needles from water or alcohol, m. p. 221—222° (Found: C, 58·2; H, 5·4. $C_{12}H_{13}O_3N_3$ requires C, 58·3; H, 5·3%), and was hydrolysed to the amine by dilute hydrochloric acid. The amine hydrochloride, diazotised and coupled with β-naphthol, gave orange-red needles (from much acetic acid) of the *azo*-compound, m. p. 312—316° (decomp.) (Found: C, 66·5; H, 4·7. $C_{20}H_{16}O_3N_4$ requires C, 66·65; H, 4·45%).

α- *and* β-6-*Nitro*-N-*methylphthalaz*-1 : 4-*diones*.—4-Nitrophthalic anhydride (4·4 g., freshly crystallised from acetic anhydride) was suspended in glacial acetic acid (20 c.c.) and mixed slowly with methylhydrazine (2·2 g.); the yellow solution was gently boiled under reflux (½ hour), and the precipitate (3·3 g.) removed while hot; the filtrate, on standing, gave a second crop (1·7 g.). Both crops were mixtures, but the first crop gave the almost pure α-compound after only one crystallisation from acetic acid, and the second crop gave the pure acetyl derivative of the β-isomeride when acetylated and crystallised from acetic acid; from this acetyl derivative the pure β-isomeride was easily obtained by hydrolysis with warm dilute sodium hydroxide solution. The α-*nitro*-compound formed small, pale greenish-yellow, flat, rhomboidal needles or hexagonal plates (from acetic acid), m. p. 307° (decomp.; sintering from 295°) (Found: C, 48·85; H, 3·3; N, 19·4. $C_9H_7O_4N_3$ requires C, 48·85; H, 3·15; N, 19·0%), and was strongly triboelectric. It formed an orange-red sodium salt, and its *acetyl* derivative crystallised in small, very pale yellow, square prisms or hexagonal needles, m. p. 210° (previous sintering) (Found: C, 50·5; H, 3·75. $C_{11}H_9O_5N_3$ requires C, 50·2; H, 3·4%), and was easily hydrolysed by dilute sodium hydroxide solution. The β-*nitro*-compound formed bushes of saffron-yellow pointed prisms (from acetic acid), m. p. 293° (decomp.; sintering from 285°) (Found: C, 48·7; H, 3·55; N, 19·2%), and was only feebly triboelectric; it depressed the m. p. of the α-isomeride to about 255°. The sodium salt formed red needles. The *acetyl* derivative crystallised in very pale yellow, chisel-ended needles (from acetic acid), m. p. 195° (decomp.; sintering from 185°) (Found: C, 50·15; H, 3·6%), and depressed the m. p. of the α-isomeride to about 170°.

α- *and* β-6-*Amino*-N-*methylphthalaz*-1 : 4-*dione*.—These amines were prepared by reduction of the corresponding nitro-compounds by means of tin and hydrochloric acid, as described in the preparation of the 5-amino-isomerides; the reduction of the β-nitro-compound was the more rapid, but the stannichloride showed less tendency to separate; the stannichloride of the α-amino-compound formed long, thin, colourless needles. The α-*amino*-compound formed nearly colourless, rectangular needles (from acetic acid), m. p. 320° (decomp.) (Found: C, 56·3; H, 4·75. $C_9H_9O_2N_3$ requires C, 56·55; H, 4·7%); when crystallised from water, it separated in rectangular needles of a hydrate which retained $1H_2O$ when dried over phosphoric oxide but lost it at 100°; it was soluble in aqueous alkalis, but sparingly soluble in alcohol. The β-*amino*-isomeride crystallised from much water in short, rectangular, nearly colourless needles, which became anhydrous when dried over phosphoric oxide; m. p. above 360° (decomp.) (Found: C, 56·55; H, 4·75%). It was soluble in aqueous alkali, and its solution in dilute hydrochloric acid had a feeble blue fluorescence. The mixed m. p. of these two isomerides is 305—310° (decomp.).

6-*Nitro*-2 : 3-*dimethylphthalaz*-1 : 4-*dione*.—Prepared by the method described for its 5-nitro-isomeride, this *compound* formed saffron-yellow dendritic needles (from alcohol), m. p. 198—199° [Found: C, 50·9; H, 4·1; N, 18·0; *M* (in camphor), 241. $C_{10}H_9O_4N_3$ requires C, 51·05; H, 3·85; N, 17·85%; *M*, 235], readily soluble in acetic acid but only sparingly in water or alcohol. It was slowly hydrolysed by hot hydrochloric acid to 4-nitrophthalic acid and *s*-dimethylhydrazine.

6-Amino-2 : 3-dimethylphthalaz-1 : 4-dione.—This was prepared (yield, 80%) in the same way as its 5-amino-isomeride; it crystallised from water in colourless needles of the *dihydrate*, which lost its water at 100° (Found : H_2O, 14·95. $C_{10}H_{11}O_2N_3,2H_2O$ requires H_2O, 14·95%). The anhydrous *amine* formed white rhombs from alcohol, m. p. 262—263° (Found : C, 58·5; H, 6·0. $C_{10}H_{11}O_2N_3$ requires C, 58·5; H, 5·4%). Its *acetyl* derivative crystallised from water in colourless stout prisms of the *monohydrate*, m. p. 269—270° (Found : C, 54·75; H, 5·75. $C_{12}H_{13}O_3N_3,H_2O$ requires C, 54·35; H, 5·65%). The amine hydrochloride on diazotisation and coupling with β-naphthol gave the *azo*-compound in light red needles (precipitated from acetic acid by addition of hot alcohol), m. p. 270—272° (Found : C, 66·25; H, 4·6. $C_{20}H_{16}O_3N_4$ requires C, 66·65; H, 4·45%).

*4-Nitro-*N*-dimethylaminophthalimide*.—4-Nitrophthalic anhydride (3·5 g.) and *as*-dimethylhydrazine (1·15 g.) were mixed and heated with stirring for 1 hour at 100° and for a minute at 180°; the product was boiled with water and the insoluble crystals (2·3 g.) were recrystallised from alcohol. The *compound* formed saffron-yellow, chisel-ended needles, m. p. 152—153° [Found : C, 50·85; H, 3·8; N, 17·9; *M* (in camphor) 238. $C_{10}H_9O_4N_3$ requires C, 51·05; H, 3·85; N, 17·85%; *M*, 235], only slightly soluble in water but readily in acetic acid. It was stable to boiling water, but was readily hydrolysed by hot 2*N*-hydrochloric acid.

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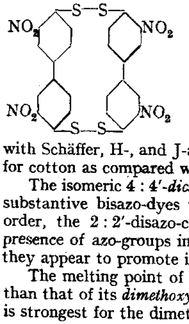
7. *Studies in the Diphenyl Series. Part IV. The Preparation and Properties of Substituted Diaminodiphenyls.*

By HERBERT H. HODGSON and PAUL F. HOLT.

THE chlorine atoms in 4 : 4′-dichloro-3 : 3′-dinitrodiphenyl (Hodgson and Walker, J., 1933, 1620) resist attack by sodium methoxide or ethoxide, but readily react with sodium disulphide, a very sparingly soluble *polysulphide* being formed, the molecular weight of which could not be determined; its analysis and properties, however, indicate the probable formula (I). The polysulphide was reduced readily to the dimercaptan, which was easily methylated to give 3 : 3′-*dinitro*-4 : 4′-*dimethylthioldiphenyl*, the reduction of which produced 3 : 3′-*diamino*-4 : 4′-*dimethylthioldiphenyl*. The latter compound and its 4 : 4′-*dimethoxy*-analogue gave rise to a series of bisazo-dyes with Schäffer, H-, and J-acids which exhibited definite but greatly reduced substantivity for cotton as compared with the isomeric 3 : 3′-disubstituted 4 : 4′-bisazo-compounds.



The isomeric 4 : 4′-*dichloro*-3 : 3′-, -2 : 3′-, and -2 : 2′-*diaminodiphenyls* likewise afforded substantive bisazo-dyes with the above intermediates, the affinity being in the above order, the 2 : 2′-disazo-compounds possessing only slight substantivity. Whereas the presence of azo-groups in the 4 : 4′-positions is therefore not essential for substantivity, they appear to promote it far more powerfully than when elsewhere in the molecule.

The melting point of 4 : 4′-*dimethylthioldiphenylene*-3 : 3′-*bisazo*-β-*naphthol* is 16° lower than that of its *dimethoxy*-analogue and indicates that chelation between the ortho-groups is strongest for the dimethylthiol derivative (cf. Hodgson and Handley, J., 1926, 542).

EXPERIMENTAL.

The Action of Sodium Disulphide on 4 : 4′-Dichloro-3 : 3′-dinitrodiphenyl.—The diphenyl (15 g.), boiled for 30 minutes under reflux with a mixture of alcohol (200 c.c.) and sodium disulphide (14·8 g.) dissolved in the minimum amount of water, afforded an insoluble yellow *polysulphide*, which did not melt at 340° but decomposed suddenly if rapidly heated to this temperature (cf. Blanksma, *Rec. trav. chim.*, 1901, **20**, 141, for the similar behaviour of 4 : 4′-dinitrodiphenyl disulphide). Prior to analysis it was extracted thoroughly with hot solvents in

the following sequence: water, alcohol, benzene, carbon disulphide, and alcohol [Found: S, 21·0. $(C_{12}H_6O_4N_2S_2)_n$ requires S, 20·9%].

3 : 3′-*Dinitro*-4 : 4′-*dimethylthioldiphenyl*.—The polysulphide, suspended in alcohol (600 c.c.), was boiled under reflux for 5 minutes with sodium (4·6 g.) and the solution was filtered as rapidly as possible and shaken immediately with excess of methyl sulphate; 3 : 3′-*dinitro*-4 : 4′-*dimethylthioldiphenyl*, precipitated as a bright yellow solid, crystallised from glacial acetic acid in yellow clusters, m. p. 262° (Found: S, 19·2. $C_{14}H_{12}O_4N_2S_2$ requires S, 19·0), only slightly soluble in alcohol.

3 : 3′-*Diamino*-4 : 4′-*dimethylthioldiphenyl*.—(*a*) Reduction of the above nitro-compound with tin and concentrated hydrochloric acid afforded pale yellow crystals of the *stannichloride* of the base, m. p. 242° after recrystallisation from hot hydrochloric acid (Found: S, 10·6. $C_{14}H_{18}N_2S_2,SnCl_6$ requires S, 10·4%). (*b*) Reduction of the above nitro-compound with iron and aqueous acetic acid afforded a product, which was dried and extracted with benzene.

3 : 3′-*Diamino*-4 : 4′-*dimethylthioldiphenyl dihydrochloride*, precipitated from the extract by hydrogen chloride and recrystallised from hydrochloric acid, formed colourless needles, m. p. 228° (Found: Cl, 20·8. $C_{14}H_{16}N_2S_2,2HCl$ requires Cl, 20·4%). The *base* could not be crystallised from alcohol, benzene or glacial acetic acid, and its solubility in the hot and the cold liquids appeared to be the same, since only a white opalescence was discerned when saturated solutions were cooled to 0°; it was purified by repeated dissolution in dilute hydrochloric acid and fractional precipitation by aqueous ammonia until the m. p. 71° remained constant (Found: S, 23·4. $C_{14}H_{16}N_2S_2$ requires S, 23·2%). The base was readily tetrazotised and then coupled with alkaline β-naphthol to give 4 : 4′-*dimethylthioldiphenylene*-3 : 3′-*bisazo*-β-*naphthol*, which separated from glacial acetic acid in red micro-crystals, m. p. 318° (Found: S, 11·2. $C_{34}H_{26}O_2N_4S_2$ requires S, 10·9%).

3 : 3′-*Dinitro*-4 : 4′-*dimethoxydiphenyl*.—3 : 3′-Dinitro-4 : 4′-dihydroxydiphenyl (4 g.), prepared by Kunze's method (*Ber.*, 1888, **21**, 3331), was mixed with potassium carbonate (5 g.) and sufficient water to form a paste and heated on the water-bath with methyl sulphate (10 c.c.) until the red colour of the potassium salt had disappeared; repeated additions of potassium carbonate and methyl sulphate alternately were made until the mass was permanently yellow; it was then extracted with hot dilute sodium hydroxide solution and with hot water, dried (4 g.), and crystallised from glacial acetic acid; m. p. 214° (Found: N, 9·4. $C_{14}H_{12}O_6N_2$ requires N, 9·2%).

3 : 3′-*Diamino*-4 : 4′-*dimethoxydiphenyl*.—The above dinitro-compound (11 g.) was boiled under reflux for 4 hours with glacial acetic acid (33 c.c.) and water (33 c.c.), excess of iron powder being added gradually, the mixture made alkaline with ammonia, and the dried solids extracted with benzene. The procedure described for the isolation of the dimethylthiol analogue then gave 3 : 3′-*diamino*-4 : 4′-*dimethoxydiphenyl dihydrochloride* in colourless needles, m. p. 262° (Found: Cl, 22·1. $C_{14}H_{16}O_2N_2,2HCl$ requires Cl, 22·4%). The *base* had m. p. 195° (Found: N, 11·7. $C_{14}H_{16}O_2N_2$ requires N, 11·5%), its *diacetyl* derivative formed colourless crystals, m. p. 330°, from glacial acetic acid (Found: N, 8·6. $C_{18}H_{20}O_4N_2$ requires N, 8·5%), and 4 : 4′-*dimethoxydiphenylene*-3 : 3′-*bisazo*-β-*naphthol* formed red micro-crystals, m. p. 334° (Found: N, 10·3. $C_{34}H_{26}O_4N_4$ requires N, 10·1%).

4 : 4′-*Dichloro*-3 : 3′-*diaminodiphenyl*, prepared by refluxing 4 : 4′-dichloro-3 : 3′-dinitrodiphenyl (5 g.) for 2 hours with iron filings (7 g.) and 50% aqueous acetic acid (30 c.c.), the mixture being worked up as described above, crystallised from alcohol in colourless plates, m. p. 133·5° (Found: Cl, 28·0. $C_{12}H_{10}N_2Cl_2$ requires Cl, 28·1%).

4 : 4′-*Dichloro*-2 : 3′-*diaminodiphenyl*, similarly obtained from 4 : 4′-dichloro-2 : 3′-dinitrodiphenyl (Dennett and Turner, J., 1926, 477), crystallised from 30% aqueous acetic acid in colourless needles, m. p. 83° (Found: Cl, 28·2. $C_{12}H_{10}N_2Cl_2$ requires Cl, 28·1%). The *diacetyl* derivative crystallised from glacial acetic acid in colourless needles, m. p. 90° (Found: Cl, 21·0. $C_{16}H_{14}O_2N_2Cl_2$ requires Cl, 21·1%).

4 : 4′-*Dichloro*-2 : 2′-*diaminodiphenyl*.—2 : 2′-Dinitrobenzidine was prepared by Täuber's method (*Ber.*, 1890, **23**, 795) and converted into 4 : 4′-dichloro-2 : 2′-dinitrodiphenyl by the method of Hodgson and Walker (J., 1933, 1620). This on reduction gave the *diamine*, which formed faint brown micro-crystals, m. p. 87° (Found: Cl, 28·0. $C_{12}H_{10}N_2Cl_2$ requires Cl, 28·1%).

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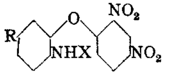
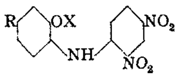
8. *A Rearrangement of* o-*Aminodiphenyl Ethers. Part V.*

By Kenneth C. Roberts and Jack A. Rhys.

In extension of the observations recorded in Parts I to IV (J., 1934, 727; 1935, 196, 1309, 1312), an investigation of the rearrangement of 5-substituted 2′ : 4′-dinitro-2-aminodiphenyl ethers (I, R = OMe, Me, H, I, Cl; X = H) to the isomeric 4-substituted diphenylamines (II) is now reported. The behaviour of certain acyl derivatives of (I and II, X = acetyl, *o*-nitrobenzoyl) is also recorded.

(I.)   (II.)

The members of the limited series which it has proved practicable to prepare show behaviour closely analogous to that of the 4-substituted ethers (*loc. cit.*, p. 727). The rates of rearrangement in minutes under the standard conditions previously described (Part II, J., 1935, 198) are shown in the accompanying table, those of the earlier 4-series being included for comparison, and the substituents being arranged in order of decreasing negative inductive effect. In the new series, approach from either side to the optimum in the neighbourhood of R = H is much more rapid, and complete inhibition of the change under the standard conditions is reached on the one hand at R = OMe and on the other at R = Cl. This is presumably due to the stronger effect of R in the *p*- than in the *m*-position to the amino-group in inhibiting the rearrangement either by reducing the tendency

Substituent (R)	NH_2	OMe	Me	H	I	Br	Cl	CO_2H
4-Series	50	13	7	5	15	30	60	No change
5-Series	—	No change	90	5	7	—	No change	—
				Decreasing		$-I$ ⟶		$+I$

of amino-hydrogen to be ejected as a proton (R = OMe) or by reducing the ability of the amino-nitrogen atom to supply the electron demand at the positive α-carbon atom in the dinitrophenyl nucleus (R = Cl). In this connection compare Part II (*loc. cit.*, p. 197) and also the generalisations of Evans and Smiles (J., 1935, 181) covering the mechanism of rearrangements of this type.

An additional feature shown in the new series is the highly specific nature of the effect of the catalysing solvent. Thus the simple alcohols which readily effect rearrangement of the 4-substituted ethers are without effect on those now discussed. A further instance of this specificity is provided by the 5-methyl ether in the present series, which, while it undergoes the normal rearrangement under the influence both of weak bases (aniline, pyridine) and of alkalis (aqueous caustic soda, baryta), is most readily affected by the strongly basic piperidine. In this solvent, which is without effect either on the 4-substituted ethers or on the other members of the present series, the 5-methyl ether is converted almost instantaneously into the isomeric diphenylamine. The 5-methoxy- and the 5-chloro-ether, which readily rearrange at their melting points, are nevertheless stable towards all other reagents tried.

Experimental.

2′ : 4′-*Dinitro*-2-*hydroxy*-4-*methoxydiphenylamine*.—2-Amino-5-methoxyphenol was conveniently prepared by reduction of an aqueous-alcoholic solution of benzeneazoresorcinol 4-methyl ether with sodium hyposulphite. It was isolated as the hydrochloride by treatment of the reaction mixture with hydrochloric acid.

Equimolecular amounts of the above hydrochloride and 1-chloro-2 : 4-dinitrobenzene in alcohol were heated for 6 hours under reflux in presence of anhydrous sodium acetate (4 mols.). The *product*, isolated in 60% yield by usual methods, exhibited chromoisomerism, being obtained red from alcoholic solution and brown from glacial acetic acid, m. p. 178° (Found: C, 51·4; H, 3·3. $C_{13}H_{11}O_6N_3$ requires C, 51·1; H, 3·6%).

2′ : 4′-*Dinitro*-2-*hydroxy*-5-*methoxydiphenyl Ether*.—2-Amino-5-methoxyphenol hydrochloride (1 mol., 1·2 g.) in alcohol (40 c.c.) containing potassium ethoxide (2 mols.) was cooled in ice,

and chlorodinitrobenzene (1 mol.) in alcohol added. After 1 hour the insoluble yellow *ether* was purified (yield 40%) and recrystallised from benzene, forming yellow needles, m. p. 162° (Found: C, 51·3; H, 3·3. $C_{13}H_{11}O_6N_3$ requires C, 51·1; H, 3·6%). No diphenylamine was observed among the products of the reaction.

2′ : 4′-*Dinitro-2-hydroxy-4-methyldiphenylamine*.—4-Amino-*m*-cresol (3 g., from 4-nitro-*m*-cresol in aqueous caustic soda with sodium hyposulphite) in alcohol (20 c.c.) was treated with chlorodinitrobenzene (5 g.) and anhydrous sodium acetate (5 g.) for 2 hours under reflux. The *product* (80% yield), isolated by pouring the reaction mixture into cold water, crystallised from alcohol in alkali-soluble red needles, m. p. 166—167° (Found: C, 53·7; H, 4·2. $C_{13}H_{11}O_5N_3$ requires C, 54·0; H, 3·8%). The substance was also obtained by rearrangement of the isomeric diphenyl ether. The orange *acetate*, m. p. 145°, was purified from alcohol (Found: C, 54·2; H, 3·4. $C_{15}H_{13}O_6N_3$ requires C, 54·3; H, 3·9%). The o-*nitrobenzoate*, prepared in acetone solution in presence of anhydrous sodium carbonate, formed bright yellow crystals, m. p. 185°, from benzene (Found: C, 54·7; H, 3·4. $C_{20}H_{14}O_8N_4$ requires C, 54·7; H, 3·1%). This substance also resulted when 2′ : 4′-dinitro-2-amino-5-methyldiphenyl ether in warm acetone was treated with excess of *o*-nitrobenzoyl chloride.

2′ : 4′-*Dinitro-2-amino-5-methyldiphenyl Ether*.—4-Amino-*m*-cresol (6 g.) in the minimum amount of alcohol was treated with sodium ethoxide (somewhat less than 1 mol.) and added to chlorodinitrobenzene (10 g.) dissolved in alcohol (80 c.c.); the mixture was kept for 1 hour at 20°. The resulting *ether*, which separated in 45% yield, formed yellow crystals, m. p. 134°, from benzene (Found: C, 53·8; H, 4·1. $C_{13}H_{11}O_5N_3$ requires C, 54·0; H, 3·8%). The isomeric diphenylamine also was isolated from the reaction mixture. The *acetyl* derivative, formed in the cold with acetic anhydride in presence of 50% aqueous acetic acid, formed pale yellow needles, m. p. 146°, from benzene (Found: N, 12·8. $C_{15}H_{13}O_6N_3$ requires N, 12·6%). The o-*nitrobenzoyl* derivative, formed in glacial acetic acid solution with *o*-nitrobenzoyl chloride at room temperature, was a white substance, m. p. 206° (from benzene) (Found: N, 12·8. $C_{20}H_{14}O_8N_4$ requires N, 12·7%).

The parent ether rearranged rapidly to the isomeric diphenylamine in piperidine solution in the cold, and also when heated alone at 150°. The same rearrangement was effected slowly in contact with 2*N*-sodium hydroxide and with 2*N*-baryta, and also in solution in aniline and in pyridine. Alcohols, organic acids and aqueous ammonia were without effect. The above derivatives underwent similar but slower rearrangements to the corresponding derivatives of the isomeric diphenylamine, the *o*-nitrobenzoyl more slowly than the acetyl derivative; but heating of the solution in some cases effected hydrolysis of the derivative.

2′ : 4′-*Dinitro-2-hydroxydiphenylamine*.—The m. p. of this material, previously recorded as 199°, is 205°.

2′ : 4′-*Dinitro-2-aminodiphenyl Ether*.—An improved yield (80%) of this substance was obtained (cf. Part II, *loc. cit.*, p. 199) by using somewhat less than the theoretical amount of sodium ethoxide in the condensation, and by keeping the reaction mixture for only ¾ hour. The m. p. is 133°, not 123° as previously reported (*loc. cit.*).

4-*Iodo*-2′ : 4′-*dinitro-2-hydroxydiphenylamine*.—A paste of *m*-iodoaniline (11 g.) with sulphuric acid (20 g.) and water (50 c.c.) was diazotised at 0° with a 10% solution of sodium nitrite (4 g.). After 2 hours the filtered liquid was added slowly to a mixture of sulphuric acid and water (2 : 1) at 140°. *m*-Iodophenol distilled in quantitative yield (cf. B.P. 200,714). 3-Iodo-6-nitrophenol (Hodgson and Moore, J., 1927, 632) in boiling 50% aqueous alcohol was quantitatively reduced by sodium hyposulphite to 3-iodo-6-aminophenol. Condensation of the latter with chlorodinitrobenzene as described above yielded the *diphenylamine* (80%; red crystals, m. p. 180°, from alcohol. Found: C, 36·2. $C_{12}H_8O_5N_3I$ requires C, 35·9%). The same substance resulted on rearrangement of the isomeric diphenyl ether. The o-*nitrobenzoate*, prepared as above, was obtained as a bright yellow substance, m. p. 206°, from benzene (Found: N, 10·2. $C_{19}H_{11}O_8N_4I$ requires N, 10·1%). It was also formed when the iodoaminodiphenyl ether in warm acetone was treated with excess of *o*-nitrobenzoyl chloride.

5-*Iodo*-2′ : 4′-*dinitro-2-aminodiphenyl Ether*.—3-Iodo-6-aminophenol (1 g.) in absolute alcohol (20 c.c.) containing potassium ethoxide (1 mol.) was treated for 1 hour at 20° with chlorodinitrobenzene (1 mol.) in the minimum amount of alcohol. The purified insoluble *product* (50% yield) was obtained after two crystallisations from benzene in bright yellow needles, m. p. 175° (Found: C, 35·8; H, 2·2. $C_{12}H_8O_5N_3I$ requires C, 35·9; H, 1·9%). A little of the isomeric diphenylamine also was formed. The o-*nitrobenzoyl* derivative, prepared in cold acetic acid solution, was a colourless substance, m. p. 194° (from benzene) (Found: N, 10·0. $C_{19}H_{11}O_8N_4I$ requires N, 10·1%).

The parent ether rearranged at the melting point, and in both aniline and pyridine solutions, but not in aqueous alkali or in piperidine. Normal rearrangement of the *o*-nitrobenzoyl derivative took place slowly under the usual conditions.

4-Chloro-2′ : 4′-dinitro-2-hydroxydiphenylamine.—To *m*-chlorophenol (13 g.) in cooled glacial acetic acid (100 c.c.) was gradually added fuming nitric acid (6·3 g.) in glacial acetic acid (100 c.c.) at 0°. The material which separated when the reaction mixture was poured on ice was distilled with steam, and the volatile 3-chloro-6-nitrophenol was thus removed in 32% yield. The chloronitrophenol in 50% aqueous alcohol was smoothly reduced by gradual addition of sodium hyposulphite (*q.s.*). After removal of alcohol, the aminophenol separated in a very pure form (yield, theoretical).

Condensation of the aminophenol to the *diphenylamine* was effected as usual, the product (90% yield) being obtained in a red form from alcohol and in purple needles from benzene, both having m. p. 208°. It was also obtained during the preparation of the isomeric diphenyl ether (below) (Found: C, 46·8; H, 2·2. $C_{12}H_8O_5N_3Cl$ requires C, 46·5; H, 2·5%). The o-*nitrobenzoate* formed yellow plates, m. p. 196°, from glacial acetic acid (Found: N, 12·2. $C_{19}H_{11}O_8N_4Cl$ requires N, 12·2%).

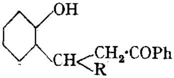
5-Chloro-2′ : 4′-dinitro-2-hydroxydiphenyl Ether.—3-Chloro-6-aminophenol (3 g.) in alcohol (20 c.c.) containing potassium ethoxide (1 mol.) was treated for 1½ hours at room temperature with chlorodinitrobenzene (1 mol.) in alcohol (40 c.c.). The insoluble yellow *ether* (yield, 70—80%) was purified from alcohol and from benzene, m. p. 176° (Found: C, 46·3; H, 2·3. $C_{12}H_8O_5N_3Cl$ requires C, 46·5; H, 2·5%). The isomeric diphenylamine also was formed in small amount. The o-*nitrobenzoyl* derivative, prepared by usual methods, formed colourless prisms, m. p. 202°, from benzene (Found: N, 12·0. $C_{19}H_{11}O_8N_4Cl$ requires N, 12·2%). It also resulted when the chlorodiphenylamine in boiling acetone was treated with excess of *o*-nitrobenzoyl chloride. For similar anomalous reactions, compare Part III, *loc. cit.*, p. 1310.

King's College, London, W.C. 2. [*Received, October 19th*, 1936.]

9. *Reactions of* o-*Hydroxybenzylidenediacetophenones. Part VII. Flavylium Salts from Dihydrochalkones.*

By A. D. Harford and Douglas W. Hill.

The mechanism of the disproportionation which takes place as a result of the action of acids upon salicylidenediacetophenones with the formation of phenacylideneflavenes is still obscure. None of the changes introduced into the structure (I; R = CH_2·COPh) have inhibited the dehydrogenation effect and it was intended to extend the investigation to compounds in which the group R had been varied. Circumstances prevent this plan being carried out and it is not proposed to continue the work. The results so far obtained are, however, of interest from other points of view and some compounds are here described in which the phenacyl group has been replaced by hydrogen.



(I.)

Of the many methods introduced for the preparation of flavylium salts, oxidation reactions have received least attention. A number of such reactions have recently been described (see Hill, *Chem. Rev.*, 1936, **19**, 37, for summary) and it seemed worth recording that the ω-salicylacetophenones investigated were converted readily into flavylium chlorides (isolated as ferrichlorides) by the action of hydrogen chloride in acetic acid without the aid of an oxidising agent. In their oxidation to flavylium salts, therefore, the salicylacetophenones behave in a manner analogous to the diacetophenones, the group R, whether H or CH_2·COPh, being removed to permit the formation of the salt. This behaviour does not extend to salicylacetone, since we were unable thus to change it, and Miller and Robinson (J., 1934, 1535) found it necessary to introduce an oxidising agent (chloranil) to effect the conversion of β-(2-hydroxy-1-naphthyl)ethyl methyl ketone into a naphthapyrylium salt.

The difference between salicylacetone and ω-salicylacetophenones is further emphasised by their respective behaviours towards attempts at cyclisation. Baker and Walker (J., 1935, 646) described the very ready cyclisation of salicylacetone to a carbinol which lost water easily to form a chromene. If the salicylacetophenones described here are to exhibit

similar changes to the salicylidenediacetophenones, they must do so with the formation of a dimer through the intermediate carbinols and chromenes resembling the product of Baker and Walker. No evidence has been found for any of these compounds.

ω-Salicylacetophenone, *4-methoxy-ω-salicylacetophenone*, and *3′ : 4-dimethoxy-ω-salicylacetophenone*, unlike salicylacetone, could not be cyclised by any of the methods adopted by Baker and Walker. They were unaffected by acids, and the action of acetic anhydride led only to the formation of *acetyl* derivatives, as with hydroxychalkones themselves (Zwayer and Kostanecki, *Ber.*, 1908, **41**, 1337).

EXPERIMENTAL.

4-Methoxy-ω-salicylacetophenone.—A solution of 4-methoxysalicylideneacetophenone (5 g.) in warm methyl alcohol (300 c.c.) was reduced by shaking with hydrogen in the presence of Adams's platinum oxide catalyst (0·1 g.). The required volume of hydrogen was rapidly absorbed and the previously yellow solution became colourless. It was filtered from the catalyst and evaporated to 50 c.c., and sufficient water added to produce a turbidity. On standing, colourless hard rhombs separated, which were recrystallised from alcohol and water; m. p. 64—65° (Found : C, 75·0; H, 6·3. $C_{16}H_{16}O_3$ requires C, 75·0; H, 6·3%). The *phenylhydrazone* formed almost colourless needles from aqueous alcohol, m. p. 140—141° (Found : N, 7·5. $C_{22}H_{22}O_2N_2$ requires N, 8·0%).

3′ : 4-Dimethoxy-ω-salicylacetophenone.—A solution of 3′ : 4-dimethoxysalicylideneacetophenone (5 g.) in warm methyl alcohol (300 c.c.) was treated as described above. The colourless solution was evaporated to low bulk and allowed to crystallise. The *product*, recrystallised twice from alcohol, formed colourless needles, m. p. 89—90° (Found : C, 71·1; H, 6·35. $C_{17}H_{18}O_4$ requires C, 71·3; H, 6·3%). The *phenylhydrazone* crystallised in very pale yellow needles from alcohol, m. p. 145—146° (Found : N, 7·55. $C_{23}H_{24}O_3N_2$ requires N, 7·45%).

Flavylium Ferrichloride from ω-Salicylacetophenone.—Hydrogen chloride was passed through a suspension of salicylacetophenone (1 g.) in glacial acetic acid (10 c.c.) for 5 minutes. All the solid had then dissolved and the solution assumed a deep red colour. Ferric chloride in glacial acetic acid (0·5 g. in 7 c.c.) was added to the mixture, which soon began to deposit yellow plates. These, when crystallised from glacial acetic acid, had m. p. 138—140° (flavylium ferrichloride has m. p. 138—140°).

4′-Methoxyflavylium Ferrichloride from 4-Methoxy-ω-salicylacetophenone.—By the same treatment 4-methoxysalicylacetophenone (1 g.), suspended in glacial acetic acid (10 c.c.), was converted into 4′-methoxyflavylium ferrichloride, obtained as orange-coloured blades from glacial acetic acid, m. p. 155—156° (Perkin, Robinson, and Turner, J., 1908, **93**, 1112, give m. p. 156°).

8 : 4′-Dimethoxyflavylium Ferrichloride from 3′ : 4-Dimethoxy-ω-salicylacetophenone.—3′ : 4-Dimethoxysalicylacetophenone (1 g.), suspended in glacial acetic acid (10 c.c.), was treated as above. The deep red solution on treatment with ferric chloride (0·5 g. in 6 c.c. of glacial acetic acid) yielded a solid, which separated from glacial acetic acid in fine red needles, m. p. 178° (Robinson and Williams, J., 1924, **125**, 209, give m. p. 180°).

O-*Acetyl-ω-salicylacetophenone.*—Salicylacetophenone (3 g.) was refluxed for 2 hours with acetic anhydride (20 c.c.), and the solution then poured into water. The thick oil remaining after the acetic anhydride had been decomposed was extracted with ether, and the extract washed with sodium carbonate solution, dried over anhydrous sodium sulphate, and evaporated. The residue crystallised from alcohol in colourless needles, m. p. 65° (Found : C, 76·1; H, 6·1. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%).

O-*Acetyl-4-methoxy-ω-salicylacetophenone.*—By the same procedure, 4-methoxy-ω-salicylacetophenone (1·5 g.) was converted into its *acetyl* derivative, which separated from alcohol in colourless plates, m. p. 84—85° (Found : C, 72·5; H, 6·4. $C_{18}H_{18}O_4$ requires C, 72·5; H, 6·1%).

O-*Acetyl-3′ : 4-dimethoxy-ω-salicylacetophenone.*—3′ : 4-Dimethoxy-ω-salicylacetophenone (2 g.) was refluxed with acetic anhydride (15 c.c.) for 1 hour, and the mixture treated as above. The *acetyl* derivative separated from alcohol, after long standing, in colourless needles, m. p. 55—56° (Found : C, 69·4; H, 6·3. $C_{19}H_{20}O_5$ requires C, 69·5; H, 6·1%).

Refluxing with glacial acetic acid had no effect on any of the salicylacetophenones described above, nor had hydrogen chloride in alcohol.

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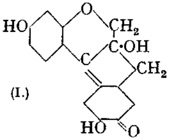
UNIVERSITY COLLEGE, EXETER. [*Received, October 22nd*, **1936**.]

10. *The Constitution of Brazilein.*

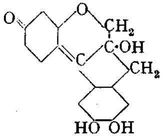
By V. M. Mićović and Robert Robinson.

The methylation of brazilein by means of methyl sulphate and potassium hydroxide affords trimethylbrazilein, tetramethyldihydrobrazileinol and a dimethylbrazilein which has phenolic properties (Engels, Perkin, and Robinson, J., 1908, **93**, 1115). The formation of the last substance in considerable relative amount was held to favour (I) rather than the alternative (II) as a representation of the structure of brazilein. This argument lacked precision and no confirmatory evidence was available. Indeed Pfeiffer (cf. Meyer and Jacobson, " Lehrbuch d. Org. Chem.," V, 1, 197) has put forward the suggestion that brazilein is (II), a view not supported by any new experimental data.

We have now been able to demonstrate that *O*-trimethylbrazilein, of known constitution in other respects, is a derivation of (I) rather than of (II), and hence brazilein should be (I). As in the case of other potentially tautomeric systems immobilised by substitution, we can determine the structure of the derivative alone with certainty. Nevertheless in the present example it will be agreed that brazilein very probably affords a true trimethyl ether and no isomeride of this derivative has been isolated.

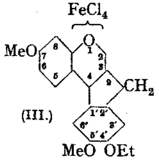


(I.)

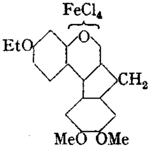


(II.)

The hydration of the quinonoid group of trimethylbrazilein probably gives rise to stereoisomerides, of which one is produced in predominating amount; this trimethyldihydrobrazileinol affords a crystalline *ethyl ether*. On gentle heating of the solution of this substance in concentrated sulphuric acid, the *dimethoxyethoxybrazylium* * *acid sulphate* is produced and this salt is precipitated on the addition of water. It was converted in the usual manner into a related *ferrichloride*, which might have structure (III) or (IV) according as trimethylbrazilein is based on (I) or (II) respectively. The salts (III) and (IV) have therefore been synthesised and, although they closely resembled one another, it was found possible to distinguish between them—a matter requiring special attention.



(III.)



(IV.)

The ferrichloride (III) was found to be identical with the salt obtained from brazilein as described above. The methods employed for the syntheses were adaptations of those already recorded in connection with trimethoxybrazylium salts. Thus (III) was derived from a *deoxydimethylethylbrazilone* prepared from *O-ethyl*iso*vanillylidene-7-methoxychroman-*

* It seems desirable to abandon the use of the expressions *iso*brazilein and *iso*hæmatein, because these substances are really anhydrobrazilein and anhydrohæmatein. Their salts are pyrylium derivatives and, as a considerable number are known, it is suggested that 4 : 3-indenobenzopyrylium (1 : 4) of earlier memoirs [more correctly designated indeno(2′ : 3′ : 3 : 4)benzopyrylium] may be termed *brazylium*. The numbering is by analogy to that used for *flavylium*, despite the fact that substitution or addition at 3, 4, 1′ and 2′ is impossible. The so-called *iso*hæmatein salts now become derivatives of tetrahydroxybrazylium.

one following the stages of the method contemporaneously worked out by Pfeiffer and hi collaborators (*Ber.*, 1917, **50**, 911; 1920, **53**, 945; 1925, **58**, 1947; 1928, **61**, 1923) and by Perkin, Rây, and Robinson (J., 1926, 941; 1928, 1504. Cf. *Proc. Chem. Soc.*, 1906, **22** 160). The earlier synthesis of Crabtree and Robinson (J., 1918, **113**, 859) was suitably modified for the preparation of (IV).

Except as indicated below, this investigation was completed in 1931 but it was found impossible to reach a definite conclusion because the ferrichlorides from the three sources (from brazilein and the two syntheses) differed in appearance and habit of crystallisation. This has quite recently been found to be due to traces of foreign substances, especially iodine, in the product obtained from brazilein, and bromine in the synthetic salt (III).

Prevention proved better than cure, and the observance of some simple precautions enabled us to equate (III) (synthetic) in all respects with the salt from brazilein. Several analytically pure specimens of the salt (IV) have been examined and although these differed somewhat from one another in appearance in mass, the crystalline forms were identical and the melting points (decomp.) were the same and 8—10° higher than that of (III). Mixtures of (III) and (IV) (all specimens) showed a depressed melting point.

EXPERIMENTAL.

ω-Homoveratrylresacetophenone.—The following method of preparation of this substance is superior to that previously described (Baker and Robinson, J., 1925, **127**, 1433). A mixture of β-veratrylpropionitrile (19·1 g.), resorcinol (11 g.), zinc chloride (4 g.), and dry ether (100 c.c.) was saturated at 0° with dry hydrogen chloride during 1 hour and kept for 40 hours. The solid product was washed with ether and dissolved in ice-water, and the solution extracted with ether in order to remove unchanged substance and then decomposed by boiling for 15 minutes. After crystallisation from methyl alcohol the ketone had m. p. 146—147° (10·5 g. or 35%).

β-Veratrylethyl 2-Hydroxy-4-ethoxyphenyl Ketone.—Ethyl iodide (7 g.) was added to a solution of the sodium salt obtained from sodium (0·9 g.), alcohol (100 c.c.), and homoveratrylresacetophenone (11·5 g.), and the mixture was refluxed for 4 hours. Alcohol was removed and dilute aqueous sodium hydroxide was added to the residue, a solid being precipitated. This crystallised from methyl alcohol in prismatic needles, m. p. 97—98° (Found: C, 69·1; H, 6·8; MeO,* 18·7; EtO,* 13·6. $C_{19}H_{22}O_5$ requires C, 69·1; H, 6·7; 2MeO, 18·8; EtO, 13·6%). The same *substance* was obtained by condensation of β-veratrylpropionitrile and *m*-ethoxyphenol by means of hydrogen chloride in presence of zinc chloride, which shows that the condensation occurs in the *o*-position to the phenolic hydroxyl group.

4′ : 5′-Dimethoxy-7-ethoxybrazylium Ferrichloride (IV).—A mixture of homoveratrylresacetophenone ethyl ether (6·6 g.), fused zinc chloride (10 g.), and anhydrous formic acid (40 g.) was refluxed for 6 hours. After cooling, dilute hydrochloric acid and an excess of ferric chloride dissolved in 20% hydrochloric acid were added, whereby a dark mass was precipitated. After collection this crystallised from acetic acid in glistening, chocolate-coloured needles (Found: C, 46·6; H, 3·6; Cl, 26·2; Fe, 10·3; MeO, 11·8; EtO, 8·6. $C_{20}H_{19}O_4Cl_4Fe$ requires C, 46·1; H, 3·7; Cl, 27·2; Fe, 10·7; 2MeO, 11·5; EtO, 8·4%). The *substance* loses chlorine on further crystallisation from glacial acetic acid (Found: C, 46·9; H, 3·8; Cl, 26·1; Fe, 10·0%). It was, however, obtained in a pure condition by solution in the minimum of hot absolute formic acid and addition of 2 volumes of glacial acetic acid containing a trace of ferric chloride and of hydrogen chloride. In this way slender orange needles, m. p. 211—212° (decomp.), could be consistently obtained (Found: C, 46·2; H, 3·7; Cl, 27·1%). A description of the properties of this salt (specimen A) is given below.

7-Methoxy-3-(4′-methoxy-3′-ethoxybenzylidene)chromanone.—A solution of 7-methoxychromanone (3·6 g.) (Perkin, Rây, and Robinson, J., 1927, 2097) and *O*-ethyl*iso*vanillin (3·6 g.) in acetic acid (20 c.c.) was saturated with dry hydrogen chloride at 0°. Next day the product was decomposed with crushed ice and the solid collected and crystallised from methyl alcohol, from which it separated in pale yellow needles, m. p. 120° (5 g. or 73·5%) (Found: C, 70·7; H, 5·9. $C_{20}H_{20}O_5$ requires C, 70·6; H, 5·9%).

7-Methoxy-3-(4′-methoxy-3′-ethoxybenzyl)chromanone.—A solution of methoxyethoxybenzylidenechromanone (1·7 g.) in ethyl acetate (100 c.c.), to which norit (2 g.) and palladous chloride (15 c.c. of 0·5% aqueous solution) had been added, was shaken with hydrogen. 130 C.c. of the gas were absorbed at 23° in 12 minutes. The operation was stopped, the liquids were

* Calc. on the assumption 2MeO : 1EtO.

filtered, and the separated ethyl acetate solution was evaporated under diminished pressure. The reduction *product* was crystallised from aqueous methyl alcohol and then from methyl alcohol; it formed colourless prisms, m. p. 83° (Found : C, 70·0; H, 6·4. $C_{20}H_{22}O_4$ requires C, 70·1; H, 6·5%).

When methoxyethoxybenzylidenechromanone (0·8 g.) was reduced under similar conditions for a longer period, *7-methoxy-3-(4'-methoxy-3'-ethoxybenzyl)chromanone* was obtained. 160 C.c. of hydrogen were absorbed during 40 minutes and further absorption did not occur. The colourless product, crystallised from aqueous methyl alcohol, had m. p. 87—90° (Found : C, 73·0; H, 7·5. $C_{20}H_{24}O_4$ requires C, 73·1; H, 7·4%).

Deoxydimethylethylbrazilone.—Phosphoric oxide (5 g.) was added to a solution of the above ketone (1 g.) in benzene (10 c.c.); the mixture was well shaken and gently refluxed during 2 hours. More phosphoric oxide (*ca.* 1 g.) was then added, and the operation repeated after 2 hours. After 12 hours the mixture was decomposed with ice and extracted with ether with the addition of salt, the ethereal solution washed with water and aqueous sodium hydroxide, dried with potassium carbonate and filtered, and the solvent removed. The residue, crystallised from methyl alcohol, had m. p. 145—147° (yield, 14%) (Found : C, 74·0; H, 6·2. $C_{20}H_{20}O_4$ requires C, 74·1; H, 6·2%). This *substance* closely resembles deoxytrimethylbrazilone in all its characteristic properties.

7 : 5'-*Dimethoxy-4'-ethoxybrazylium Ferrichloride* (III).—The foregoing synthetic deoxydimethylethylbrazilone (0·85 g.) was dissolved in acetone (25 c.c.), and the solution shaken with bromine vapour mixed with a large relative volume of air. A crimson coloration was produced and this gradually faded and was replaced by an orange colour; a trace more bromine was then introduced in the same way and so on until the red colour was no longer observed. It is important to avoid excess of bromine at any stage and as the reaction proceeds the dimethoxyethoxybrazylium bromide separates in orange microscopic prismatic needles. After the addition of dry ether, the salt was collected (0·9 g.), dissolved in the minimum of alcoholic hydrogen chloride (10%), and mixed with a large excess of ferric chloride dissolved in concentrated hydrochloric acid. An orange-brown ferrichloride was precipitated and was crystallised from acetic acid containing a trace of hydrogen chloride and a trace of ferric chloride. The orange-brown prismatic needles were orange by transmitted light under the microscope (specimen B). When a concentrated solution in anhydrous formic acid was mixed with twice its volume of acetic acid, long, slender, microscopic needles and obliquely cut, prismatic needles separated. Less pure specimens crystallise in rosettes of slender needles. Recrystallisation is attended by some decomposition and the above specimen (B) was the purest obtained; its properties are described below (Found : C, 46·0; H, 3·6; Cl, 27·0; Fe, 10·5. $C_{20}H_{19}O_4Cl_4Fe$ requires C, 46·1; H, 3·7; Cl, 27·2; Fe, 10·7%).

O-*Trimethylethyldihydrobrazileinol.*—For the preparation of this substance it is necessary to employ pure crystallised trimethyldihydrobrazileinol, m. p. 182—185° (cf. Engels, Perkin, and Robinson, *loc. cit.*, p. 1137); otherwise the ethyl ether is obtained as an uncrystallisable gum.

A mixture of trimethyldihydrobrazileinol (5 g.), ethyl iodide (25 c.c.), acetone (50 c.c.), and powdered potassium carbonate (20 g.) was refluxed for 2 hours, then cooled, and mixed with ether and water and the ethereal solution was washed several times with dilute aqueous sodium hydroxide. The residue, after removal of ether from the dried solution, crystallised from benzene–light petroleum in slender colourless needles, which were recrystallised from methyl alcohol and then had m. p. 142° (Found : C, 67·7; H, 6·2. $C_{21}H_{24}O_6$ requires C, 67·8; H, 6·4%). This *substance* closely resembles tetramethyldihydrobrazileinol in its properties, but shows a much greater tendency to crystallise. In view of the fact that the highest m. p. recorded for the tetramethyl ether is 55—60°, it would appear that a homogeneous specimen has not yet been obtained. There is obviously a possibility of the formation of stereoisomerides when the quinonoid group of trimethylbrazilein is hydrated. Trimethylethyldihydrobrazileinol dissolved in anhydrous formic acid to an intense crimson solution exhibiting a weak green fluorescence; it was recovered unchanged on the addition of water.

Dimethoxyethoxybrazylium Ferrichloride (from Brazilein).—O-Trimethylethyldihydrobrazileinol (1·5 g.) was dissolved in sulphuric acid (40 c.c.), and the crimson solution heated to 40—50°; it then quickly became orange in colour and acquired a brilliant yellowish-green fluorescence. When the crimson colour had been discharged, the oxonium sulphate, precipitated on the addition of ice (200 g.), was collected and dissolved in alcoholic hydrogen chloride (7%), and the chloride precipitated by the addition of 5% hydrochloric acid; this process was repeated and the crude chloride was washed with a little alcoholic hydrogen chloride (10%). The salt

was then converted into ferrichloride in the usual manner; this derivative crystallised from acetic acid containing traces of hydrogen chloride and ferric chloride in brownish-orange needles (specimen C) (Found: C, 46·0; H, 3·7; Cl, 26·9; Fe, 10·5. $C_{20}H_{19}O_4Cl_4Fe$ requires C, 46·1; H, 3·7; Cl, 27·2; Fe, 10·7%).

Comparison of the Specimens A, B and C.—The three specimens closely resembled the known trimethoxybrazylium ferrichloride in all general properties; the yellow aqueous solutions exhibited intense green fluorescences identical to visual observation. The behaviour with nitric acid (cf. Crabtree and Robinson, *loc. cit.*) was also the same in the three cases and the only superficial differences that could be noted were the following :—

On heating solutions of (A), (B) or (C) in sulphuric acid, they darkened, became brown and acquired a much deeper intense green fluorescence; at equivalent concentrations (A) underwent these changes more rapidly than (B) or (C), which behaved alike. The solubilities of (B) and (C) in formic acid were similar and crystallisation on the addition of acetic acid synchronised in the case of parallel experiments; on the other hand (A) was less soluble in formic acid than (B) or (C) and crystallisation on the addition of acetic acid was more rapid.

The crystal forms were variable and dependent on the purity of the specimens. Actually both (B) and (C) crystallised in characteristic prismatic needles, but other specimens of these salts occurred as rosettes of slender needles or as thicker pointed needles. Mixtures of the pure salts and less pure specimens recrystallised as the intermediate thicker needle form and it is interesting that this was found to be true of (B) mixed with less pure (C) and of (C) mixed with less pure (B). (A) always crystallised in slender needles and mixtures with (B) or (C) gave a splintered-needle form on recrystallisation. On heating, (A) began to shrink at 212° and melted with decomposition at 212—217°; after recrystallisation (A) had m. p. 210—211°, indicating slight deterioration. Both (B) and (C) had m. p. 202—204° (decomp.) after sintering at 198° and a mixture showed the same behaviour. A mixture of (A) and (B) had m. p. 187—189° (decomp.) and one of (A) and (C) had m. p. 188—190° (decomp.); the decomposition was only slight if the capillary tube was at once withdrawn from the bath.

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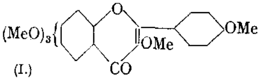
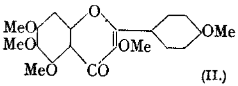
11. *A Synthesis of Tangeritin.*

By L. J. Goldsworthy and Robert Robinson.

Tangeritin, a pentamethoxyflavone, was isolated by Nelson (*J. Amer. Chem. Soc.*, **1934**, **56**, 1392) from the oil expressed from the peel of tangerine oranges (*Citrus nobilis deliciosa*) and its constitution was all but completely elucidated. On hydrolysis with aqueous alcoholic potassium hydroxide, anisic acid and tangeretol, an isomeride of gossypitol tetramethyl ether, $C_6H(OMe)_3(OH)(CO{\cdot}CH_2{\cdot}OMe)$, were obtained. The position of the extra-nuclear methoxyl in the last-named substance was not deduced as the result of further degradation but from the fact that the pentahydroxyflavone obtained by demethylating tangeritin was found to exhibit the general character of a flavonol. For these reasons tangeritin was considered to be best represented by the expression (I).



(I.)



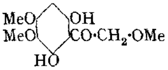
(II.)

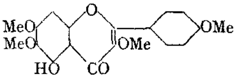
As the gossypetin-type orientation of the tetrahydroxybenzene nucleus may be tentatively excluded, it appeared that the most probable formula for tangeritin would be (II), which is structurally similar to quercetagetin, baicalein and scutellarein. Hence tangeretol should be quercetagetol tetramethyl ether and in order to correlate tangeritin and quercetagetin we tried to obtain tangeritol from *O*-hexamethylquercetagetin. The experiment was necessary because A. G. Perkin (J., **1913**, **103**, 209) used *O*-hexaethylquercetagetin in his work on the constitution of the flavonol. Owing to the small quantity of quercetagetin available, the derived *O*-tetramethylquercetagetol oxime could not be

obtained quite pure, but a mixture with tangeretol oxime had a higher melting point and there is no doubt that the two specimens were identical.

The synthesis of tangeritin was effected several months before the period of the above experiment and it followed the lines of that of quercetagetin and its pentamethyl ether (Baker, Nodzu, and Robinson, J., 1929, 76), anisic acid derivatives being substituted for those of veratric acid previously employed.

It may be recalled that the intermediate in this synthesis was a ketone obtained by coupling 4 : 5-dimethoxyresorcinol with methoxyacetonitrile in a Hoesch reaction. On grounds of analogy this was at first thought to be 4 : 6-dihydroxy-ω : 2 : 3-trimethoxyacetophenone, but this view was discarded in favour of the constitution (III) (2 : 6-dihydroxy-ω : 2 : 3-trimethoxyacetophenone) partly on account of the properties of the synthetic quercetagetin pentamethyl ether and partly as the result of further work in the same field (Baker and Robinson, J., 1929, 156).

(III.) 

 (IV.)

Naturally, if (III) had the alternative constitution, there would be no ambiguity about the orientation of hydroxyl groups in the flavones resulting from it. In the case of (III), however, there is some dubiety, resolved so far as quercetagetin is concerned by the independent unambiguous synthesis of gossypetin. In the present instance we rely on the same evidence; we assume that the direction of ring-closure using anisic anhydride with (III) will be the same as that observed when veratric anhydride was used, and we are confirmed in our view by the character of the pentahydroxyflavone produced on demethylation of the synthetic product, since this resembles quercetagetin and differs from gossypetin in its properties.

Fusion of (III) with anisic anhydride and sodium anisate, followed by hydrolysis, is accordingly considered to give *5-hydroxy-3 : 6 : 7 : 4′-tetramethoxyflavone* (IV) and on further methylation tangeritin was obtained. Through the kindness of Dr. E. K. Nelson, to whom we are greatly indebted, we have been able to make a direct comparison of the natural and the synthetical specimen, which proved to be identical.

We have taken the opportunity to prepare and more closely to characterise 3 : 5 : 6 : 7 : 4′-pentahydroxyflavone, as it would be surprising if this substance were not a natural product. The isomeric 3 : 5 : 7 : 8 : 4′-pentahydroxyflavone is being synthesised for comparison and in order to strengthen the argument bearing on the structure. We are informed by Dr. T. R. Seshadri that the flavonol herbacetin isolated by him may have this gossypetin-like constitution.

Experimental.

5-Hydroxy-3 : 6 : 7 : 4′-tetramethoxyflavone (IV).—An intimate mixture of 2 : 6-dihydroxy-ω : 3 : 4-trimethoxyacetophenone (0·5 g.), prepared essentially according to the methods described by Chapman, Perkin, and Robinson (J., 1927, 3031) and by Baker and Robinson (*loc. cit.*), anisic anhydride (2·0 g.), and sodium anisate (1·0 g.) was heated for 3 hours at 180—185° (oil-bath) under diminished pressure (20 mm.). The product of the reaction was hydrolysed by heating with alcohol (15 c.c.), water (1 c.c.), and potassium hydroxide (2·0 g.) on the steam-bath for 30 minutes, and the flavonol derivative precipitated from the cooled solution, after dilution with water (100 c.c.), by carbon dioxide; the washed and dried material (0·66 g.) had m. p. 145—150°. Two crystallisations from alcohol afforded well-defined rectangular yellow plates, m. p. 171° (Found in material dried at 120°: C, 64·0; H, 5·1. $C_{19}H_{18}O_7$ requires C, 63·7; H, 5·0%). The yellow solution of the *substance* in concentrated sulphuric acid is non-fluorescent; the ferric reaction in alcoholic solution is olive-green. The low melting point of the substance before recrystallisation suggested that it might be a mixture of the two theoretically possible products of the condensation, *viz.*, 5-hydroxy-3 : 6 : 7 : 4′-tetramethoxy- and 5-hydroxy-3 : 7 : 8 : 4′-tetramethoxy-flavone. This seemed probable in view of the fact that Baker, Nodzu, and Robinson (*loc. cit.*) obtained evidence that the analogous condensation of 2 : 6-dihydroxy-ω : 3 : 4-trimethoxyacetophenone with veratric anhydride and sodium veratrate

gave a mixed product. Accordingly an attempt was made to obtain an isomeride of the compound, m. p. 171°, from the alcoholic mother-liquors. Although various solvents, including acetic acid, ethyl acetate, acetone, mixtures of alcohol and water, and acetic acid and water were tried, all attempts to obtain a pure substance from the material derived from the mother-liquors were unsuccessful. In some cases the crystallised product melted over a range of only a few degrees, and in others over a range of 10° or more. A specimen having m. p. 145—148° (Found : C, 63·6; H, 5·2%) was probably of the nature of a eutectic mixture. The material contained in these mother-liquors was also per-methylated and gave a product, m. p. 130—137°, not appreciably raised by crystallisation from ethyl acetate. Further recrystallisations resulted in the separation of a little crude tangeritin, m. p. 150—151°, but the isomeride could not be isolated.

3 : 5 : 6 : 7 : 4′-*Pentamethoxyflavone (Tangeritin)*.—As the hydroxyl group in position 5 is known to resist methylation, the methylation of 5-hydroxy-3 : 6 : 7 : 4′-tetramethoxyflavone was carried out by the method applied by Baker and Robinson (J., 1928, 3115) to the case of 5-hydroxy-7 : 4′-dimethoxy-2-styryl*iso*flavone. Methyl sulphate (2 c.c.) and aqueous sodium hydroxide (2 c.c. of 20%) were added to a solution of 5-hydroxy-3 : 6 : 7 : 4′-tetramethoxyflavone (0·2 g.) in acetone (10 c.c.), and the mixture was shaken vigorously at about 50°. When the acetone layer, at first orange, became pale yellow, methyl sulphate (1 c.c.) and aqueous sodium hydroxide (1 c.c. of 20%) were added and the shaking was continued. On further shaking with an additional quantity of aqueous sodium hydroxide (2 c.c. of 20%) and subsequent addition of water (12 c.c.), the methylated product separated as fine white needles (m. p. 153—154°). The substance crystallised from ethyl acetate as well-defined rods and needles, m. p. 154° (Found in material dried at 100° : C, 64·4; H, 5·4. Calc. for $C_{20}H_{20}O_7$: C, 64·5; H, 5·4%) alone, or mixed with the pure specimen of tangeritin supplied by Dr. E. K. Nelson. Its solubility properties in solvents and reagents, the formation of yellow needles of an oxonium salt with concentrated hydrochloric acid, the development of a blood-red colour with concentrated nitric acid, and other characters were found on direct comparison to tally with the corresponding properties of naturally occurring tangeritin.

The synthetic product was demethylated by heating at 135° with hydriodic acid (*d* 1·7) and phenol. The yellow microcrystalline substance precipitated on the addition of sulphurous acid rapidly acquired a greenish tinge when exposed to the air.

Like the flavonol from natural tangeritin, the synthetic flavonol developed a pinkish-red colour when reduced with magnesium ribbon in an acidified alcoholic solution. Addition of an alcoholic solution of lead acetate to its alcoholic solution gave an orange-coloured precipitate, which gradually became greenish-brown. In the case of the pentahydroxy-compound from natural tangeritin this colour change is described as taking place at once. With ferric chloride an alcoholic solution of the synthetic flavonol gave a dark olive-green colour. In the case of demethylated natural tangeritin the colour is described as bluish-green. These details are given in this place because they complete the comparison of our synthetic tangeritin with the substance isolated by Nelson (*loc. cit.*). Other properties of pure 3 : 5 : 6 : 7 : 4′-pentahydroxyflavone are mentioned below.

3 : 5 : 6 : 7 : 4′-*Pentahydroxyflavone*.—A mixture of 5-hydroxy-3 : 6 : 7 : 4′-tetramethoxyflavone (0·5 g.), hydriodic acid (7·5 c.c., *d* 1·7), and phenol (2·0 g.) was heated at 135—140° for 1½ hours. The yellow needles of the hydriodide which separated were collected, triturated with sulphurous acid, and then digested for 1 hour with 50% acetic acid. Well-defined, yellow, microscopic needles were obtained in this way (Found in material dried in a vacuum : C, 59·9; H, 3·7. $C_{15}H_{10}O_7$ requires C, 59·6; H, 3·3%). On heating, the substance darkened at 270° and began to melt at about 314°; at 320° the colour was almost black and fusion was not complete.

The colour changes which accompany the oxidation of the flavonol in alkaline buffered solutions showed a general resemblance to those characteristic of quercetagetin under similar conditions (cf. Baker, Nodzu, and Robinson, *loc. cit.*), thus affording further evidence of the parallel course of the synthesis herein described and that of quercetagetin. The solutions were prepared with the aid of the " B.D.H. Universal Buffer " mixtures and were aerated before the introduction of the flavonol.

At p_H 9·8 the yellow colour of the solution changed within a few minutes to greenish-yellow and within 12 minutes to bright green; 5 minutes later the green had a distinct olive tinge, which slowly deepened and then changed to yellowish-brown, after which no further colour change occurred during 2 days.

At p_H 10·4 the same series of colour changes occurred with much greater rapidity. The

change from yellow to bright green took place in 3 minutes and within 10 minutes the colour was dark olive-green. The yellow-brown colour finally attained after several hours remained unchanged after 2 days.

At p_H 11·0 precisely similar colour changes occurred; within 6 minutes the shade of olive-green was darker than the shade observed at p_H 10·4 after 10 minutes.

The flavonol is a weaker adjective dye than quercetagetin, giving duller but generally similar shades on mordanted cotton, and the colours observed were the following: With a weak aluminium mordant, a very poor dull yellow; strong aluminium, canary-yellow; weak iron, brownish greenish grey; strong iron, deep brown; iron with aluminium, khaki.

Tangeretol Oxime from Quercetagetin.—A mixture of *O*-hexamethylquercetagetin (0·3 g.), alcohol (10 c.c.), water (7 c.c.), and potassium hydroxide (5 g.) was refluxed for 6 hours. Hydroxylamine hydrochloride (6 g.) was then introduced, and the alcohol removed by distillation; water (about 30 c.c.) was added during this process. The solution was acidified and extracted with a relatively large volume of light petroleum. The residue after removal of the solvent was a colourless viscous liquid; it was taken up in a little hot carbon disulphide, leaving a small insoluble portion, mixed with light petroleum, and on keeping in the ice-chest the solution deposited first an oil and then a small quantity of soft, colourless needles, m. p. 85—87°. The melting point was a degree higher on admixture with tangeretol oxime prepared as described by Nelson (*loc. cit.*).

Dyson Perrins Laboratory, Oxford University. [*Received, November 18th*, 1936.]

12. *Experiments on the Synthesis of Brazilin and Hæmatoxylin. Part IV. Synthesis of* O-*Diethylenehæmatoxylone.*

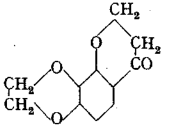
By (the late) W. H. Perkin, jun., A. Pollard, and Robert Robinson.

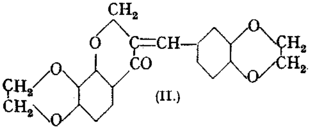
In 1928 (J., 1504, footnote) we mentioned that the investigation herein described had been completed, but we reserved publication in the hope of further developments. As, however, the hoped-for conversion of deoxytrimethylbrazilone into trimethylbrazilin or analogous transformations in the hæmatoxylin series have not been realised, the present account is submitted in order to complete the record.

The method of synthesis is that of Perkin and Robinson (*Proc.*, 1912, **28**, 7) and Perkin, Rây, and Robinson (J., 1926, 94; 1927, 2094; 1928, 1504) contemporaneously developed by Pfeiffer and his collaborators (Pfeiffer and Emmer, *Ber.*, 1920, **53**, 945; Pfeiffer, Angern, Haack, and Willems, *Ber.*, 1928, **61**, 839).

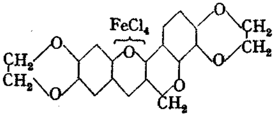
2 : 3-*Ethylenedioxy-β-phenoxypropionic acid*, $C_2H_4O_2{:}C_6H_3{\cdot}O{\cdot}CH_2{\cdot}CH_2{\cdot}CO_2H$, has been dehydrated by means of phosphoric oxide to 7 : 8-*ethylenedioxychromanone* (I), which was condensed in the usual manner with 3 : 4-ethylenedioxybenzaldehyde. The resulting *bisethylenedioxybenzylidenechromanone* (II) yields the *ferrichloride* (III) when it is treated with anhydrous ferric chloride in acetic anhydride solution. (For a proof of the constitution in an analogous case, cf. Keller and Robinson, J., 1934, 1533.)

(I.)



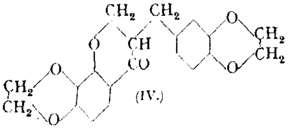


(II.)

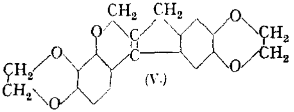


(III.)

Catalytic reduction of (II) furnishes the *dihydro*-derivative (IV), which is dehydrated by phosphoric oxide with formation of O-*diethylenedeoxyhæmatoxylone* (V). This proved to be an unsatisfactory substance, but it had the same properties as the specimen made from hæmatoxylin by a series of processes.

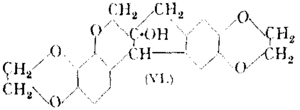


(IV.)

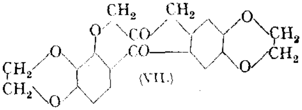


(V.)

O-*Diethylenehæmatoxylin* (VI) affords the characteristic O-*diethylenehæmatoxylone* (VII) on oxidation with chromic acid. The latter is reduced by phenylhydrazine to a product tallying with the synthetic (V).



(VI.)



(VII.)

Finally the synthetic (V) was catalytically reduced and then oxidised to diethylenehæmatoxylone identical with (VII) from hæmatoxylin.

Experimental.

2 : 3-*Ethylenedioxyphenol.*—Sodium ethoxide (sodium, 19 g.) in alcohol (275 c.c.) was added during 3½ hours with stirring under hydrogen to a mixture of pyrogallol (50 g.), alcohol (20 c.c.), and ethylene dibromide (75 g.) which was heated on the steam-bath under a reflux condenser. After boiling for a further ½ hour the alcohol was distilled, hot water was added to the residue, and after acidification the mixture was extracted with benzene. The benzene solution, after washing with water to remove unchanged pyrogallol, was dried and after removal of the solvent the residue was distilled, giving 19 g. of an almost colourless oil, b. p. 166°/25 mm., and then a bright red resin, b. p. > 300°/20 mm. The phenol was identified with that described by Magatti (*Ber.*, 1879, **12**, 1860) by preparation of the bromo-derivative.

2 : 3-*Ethylenedioxy-β-phenoxypropionic Acid.*—A solution of β-chloropropionic acid (25 g.) and sodium bicarbonate (18 g.) in water (100 c.c.) was added gradually during 1 hour to 2 : 3-ethylenedioxyphenol (30 g.) in aqueous potassium hydroxide (40 c.c. of 30%) heated on the steam-bath. After heating during 2 more hours, the solution was cooled and acidified with hydrochloric acid, and the precipitate collected and washed with water and then several times with ether. The first aqueous filtrate was extracted with ether and the combined ethereal solutions were extracted with aqueous sodium bicarbonate; acidification of these aqueous solutions afforded a further quantity of the acid. After crystallisation from alcohol, 17 g. of the *acid* were obtained and unchanged phenol was recovered from the ethereal solutions. Recrystallised from alcohol and from benzene, the acid had m. p. 156·5—158° (Found: C, 59·2; H, 5·5. $C_{11}H_{12}O_5$ requires C, 58·9; H, 5·3%).

7 : 8-*Ethylenedioxychromanone* (I).—This ketone was first prepared by heating ethylenedioxyphenoxypropionic acid with 80% sulphuric acid (cf. J., 1927, 2097), but as the yield was unsatisfactory the following method was employed.

Phosphoric oxide (50 g.) was added to a solution of the acid (15 g.) in dry benzene (350 c.c.), and the solution refluxed for 4 hours. The benzene was decanted from the dark phosphoric complex, which was decomposed by the addition of ice and the mixture was warmed and extracted with benzene. The *chromanone* was isolated as a reddish solid (11 g.), which became colourless on crystallisation from alcohol (charcoal), m. p. after recrystallisation from alcohol, 120—121° (Found: C, 64·0; H, 5·0. $C_{11}H_{10}O_4$ requires C, 64·1; H, 4·8%).

3 : 4-*Ethylenedioxybenzaldehyde.*—This compound was prepared by ethylenating protocatechualdehyde by means of sodium ethoxide and ethylene dibromide. As, however, the

yield obtained was only 20% of the theoretical, this method was abandoned and we followed Vorländer (*Annalen*, 1894, **280**, 205), Moureu (*Compt. rend.*, 1898, **126**, 1427), and Gattermann (*Annalen*, 1907, **357**, 373) with some modifications.

A mixture of pyrocatechol (100 g.) and ethylene dibromide (174 g.) was heated on the steam-bath under hydrogen, and a solution of sodium ethoxide (44 g. of sodium) in alcohol (700 c.c.) added during 3½ hours with stirring. After refluxing for a further ½ hour, the product was isolated in the known manner (67 g. of a pale yellow oil, b. p. 105°/15 mm.). The yield in the Gattermann reaction was 30%. The aldehyde forms long, silky, white needles, m. p. 51·5°.

7 : 8 : 3′ : 4′-*Bisethylenedioxy-3-benzylidenechromanone* (II).—7 : 8-Ethylenedioxychromanone (3·7 g.) and 3 : 4-ethylenedioxybenzaldehyde (4 g.) were dissolved in glacial acetic acid (30 c.c.), and the solution saturated with hydrogen chloride at 0°. After keeping at the room temperature for some hours, the solution became filled with crimson crystals, which were collected, washed with a little acetic acid, and triturated with water at about 40°; the salt then decomposed, giving the unsaturated *ketone* as a buff-coloured powder. This crystallised from ethyl acetate in pale yellow needles, m. p. 200—202° (yield, 75%) (Found: C, 68·1; H, 4·8. $C_{20}H_{16}O_6$ requires C, 68·1; H, 4·5%).

When treated in acetic anhydride solution with anhydrous ferric chloride, this substance gives an oxonium ferrichloride analogous to the one described by Perkin, Rây, and Robinson (J., 1926, 950).

Anhydrous ferric chloride (5 g.) was added to a solution of the chromanone derivative (1 g.) in acetic anhydride (25 c.c.) and after the reaction had subsided a further amount (3 g.) was added. After 10 minutes the solution was poured into water (250 c.c.) and the dark red solid was collected. On addition of a solution of ferric chloride in concentrated hydrochloric acid to the aqueous solution a further amount was obtained. Recrystallised from acetic anhydride, the ferrichloride formed garnet-red needles with a green sheen, m. p. 232—233° after softening at 229° (Found: C, 43·8; H, 2·8; Fe_2O_3, 14·5. $C_{20}H_{15}O_6Cl_4Fe$ requires C, 43·7; H, 2·8; Fe_2O_3, 14·6%).

This salt is 6 : 7 : 7′ : 8′-*bisethylenedioxychromeno*(4′ : 3′ : 2 : 3)*benzopyrylium ferrichloride* (III).

7 : 8 : 3′ : 4′-*Bisethylenedioxy-3-benzylchromanone* (IV).—An aqueous solution of palladous chloride (50 c.c. of 0·5%) with alcohol (40 c.c.) and norit (5 g., previously heated to redness) was stirred in hydrogen until no further absorption occurred. The unsaturated ketone (5 g.) in fine suspension in a mixture of ethyl acetate and alcohol (300 c.c.) was then introduced, and the solution stirred till the absorption of hydrogen slackened considerably and nearly the theoretical amount had been taken up. The solution was then filtered, concentrated to about 50 c.c., and added to water, and the white flocculent precipitate collected (80% of the theoretical). The crude *product* was dissolved in alcohol, ether added, and the solution repeatedly washed with water and then dried and concentrated; white needles separated, m. p. 130—132° (Found: C, 67·6; H, 5·2. $C_{20}H_{18}O_6$ requires C, 67·8; H, 5·1%).

Synthesis of O-*Diethylenedeoxyhæmatoxylone* (V).—After carrying out the reaction under various conditions, we found that the following gave the best results. A solution of the benzylchromanone derivative (4 g.) in dry toluene (100 c.c.) was refluxed for 2½ hours, during which time phosphoric oxide (60 g.) was added at intervals of ½ hour. The toluene solution was decanted, the residue washed several times with toluene, and crushed ice added. The phosphoric acid was neutralised with ammonia, and the toluene removed in a current of steam. After the cold mixture had been kept for some hours, a dark brown solid was collected, washed with water and with warm alcohol, and dissolved in ethyl acetate. Precipitation with light petroleum gave a flocculent brown precipitate, which was taken up in chloroform, and a solution of bromine in light petroleum added, causing the separation of a crimson solid bromide of the deoxy-compound. This was collected and shaken with zinc dust and acetic acid; the regenerated deoxy-compound was isolated as a pale yellowish-brown precipitate by pouring the acid solution into water.

A specimen which had been twice purified by conversion into the bromide and reduction by zinc dust and by aluminium amalgam separated from alcohol in pale ochreous crystals, m. p. 157° with slight previous softening, and exhibiting the same behaviour on admixture with *O*-diethylenedeoxyhæmatoxylone. The crystalline form was not characteristic, but the synthetic and the hæmatoxylin-derived specimen gave identical purple-red bromides and identical magenta colorations in benzene solution when treated with nitric acid. Their behaviour with solvents was identical in each case, both being readily soluble in chloroform, ethyl acetate, benzene and acetic acid, slightly soluble in alcohol and in hot water, and insoluble in light petroleum.

O-Diethylenehæmatoxylin (VI).—This *compound* was obtained by treating hæmatoxylin with an excess of ethylene dibromide and sodium ethoxide under the conditions employed in the preparation of 2 : 3-ethylenedioxyphenol, but the yield was only 10%. The following method gave better results. An intimate mixture of hæmatoxylin (10 g.) and finely powdered potassium carbonate (15 g.) with ethylene dibromide (20 g.) and acetone (10 c.c.) was heated in a sealed tube at 90° for 7 days. The reddish-brown mass was extracted with acetone, the solution filtered, and the acetone removed. The small amount of ethylene dibromide present was steam-distilled, leaving the hæmatoxylin ether as a brown amorphous solid (10·5 g.). The substance could not be crystallised, but it was purified by thorough washing in ethereal solution with aqueous sodium hydroxide and after recovery by repeated precipitation from benzene solution by light petroleum. The colourless flocks, freely soluble in most organic solvents, resinified on collection (Found: C, 68·0; H, 5·2. $C_{20}H_{18}O_6$ requires C, 67·8; H, 5·1%).

O-Diethylenehæmatoxylone.—*O*-Diethylenehæmatoxylin (10 g.) was dissolved in warm glacial acetic acid (60 c.c.), cooled, and a solution of chromic anhydride (5·8 g.) in a little water added gradually below 15°. A red precipitate first separated and this passed into solution as more chromic acid was added. After keeping for 2 hours, a pink solid separated, which was collected, washed with water and alcohol, and the solutions combined and diluted with water (500 c.c.), giving a further amount of materials. In the best experiments a yield of nearly 90% of the crude *diethylenehæmatoxylone* was obtained. Recrystallised from glacial acetic acid, the substance was obtained as almost colourless prisms, m. p. 198—200° (decomp.) (Found: C, 65·1; H, 4·6. $C_{20}H_{16}O_7$ requires C, 65·2; H, 4·3%).

O-Diethylenedeoxyhæmatoxylone (V).—Diethylenehæmatoxylone (4·4 g.) was added gradually to a mixture of acetic acid (20 c.c.) and phenylhydrazine (9·2 c.c.) at about 70°. After standing over-night, a certain amount of acetphenylhydrazide which had separated was collected, and the solution added to warm water. The orange-coloured precipitate was washed with warm water and cold alcohol to remove phenylhydrazine derivatives, and then dissolved in ethyl acetate. Addition of ligroin to the solution caused the separation of the *deoxy*-compound as a pale brown, flocculent mass, which was further purified by conversion into the bromide and then reduction by zinc and acetic acid. A crude specimen darkened and began to melt at 153°; when purified by separation from alcohol, it melted at 157° with slight previous softening (Found: C, 71·1; H, 4·9. $C_{20}H_{16}O_6$ requires C, 71·4; H, 4·8%). The substance resembles deoxytrimethylbrazilone and deoxytetramethylhæmatoxylone in general behaviour and some of its properties have been mentioned above.

Synthesis of O-Diethylenehæmatoxylone.—Synthetic diethylenedeoxyhæmatoxylone, purified only once through the bromide, was treated in boiling alcoholic solution with amalgamated aluminium foil for 4 hours and then recovered, the object of the treatment being the removal of traces of nuclear-substituting bromine. The colourless amorphous substance (2·1 g.) was dissolved in ethyl acetate (75 c.c.), platinum-black (0·2 g.) added, and reduction effected by shaking with pure hydrogen for 3 hours, absorption of the gas then being very slow. The product was isolated and distilled at $<$ 0·1 mm. pressure (it was impossible to observe the b. p.). The distillate (1·6 g.) was dissolved in acetic acid (30 c.c.), and chromic anhydride (2·0 g.) in a little water gradually added at about 25°; after keeping for a few hours in the ice-chest a crystalline deposit had formed and this was collected, washed with acetic acid, and crystallised from the same solvent. The colourless prismatic needles had m. p. 198—200° (decomp.) alone or mixed with diethylenehæmatoxylone prepared from hæmatoxylin (Found: C, 65·3; H, 4·5%). The specimens were identical in every respect and the characteristic reactions with alcoholic potash, sulphuric acid and nitric acid were carefully compared.

It may be noted that in earlier experiments the products of catalytic hydrogenation of natural and synthetic diethylenedeoxyhæmatoxylone (in various ways) were examined and found to be similar (m. p., *ca.* 144—146° or 154—158°, after softening at 123—126°), but the substance was never obtained in a perfectly homogeneous condition and it may be a mixture of stereoisomerides.

Other Experiments.—No pinacol could be obtained by the reduction of diethylenehæmatoxylone under various conditions.

O-Acetyldiethylenehæmatoxylin crystallised from benzene–light petroleum as elongated, colourless tablets, m. p. 132—134°.

O-Tetra-acetylhæmatoxylone crystallised from alcohol as colourless needles, m. p. 125—127°. The amorphous *O*-tetrabenzylhæmatoxylin gave an acetyl derivative from benzene–light petroleum, m. p. 112°.

O-Tetrabenzylhæmatoxylone did not crystallise, but by the action of acetic anhydride furnished acetylanhydrotetrabenzylhæmatoxylone, needles from benzene–light petroleum, m. p. 164° after sintering at 160°.

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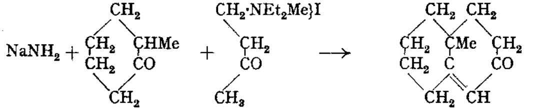
13. *Experiments on the Synthesis of Substances related to the Sterols. Part XIV. A Simple Synthesis of Certain Octalones and Ketotetrahydrohydrindenes which may be of Angle-methyl-substituted Type. A Theory of the Biogenesis of the Sterols.*

By E. C. DU FEU, F. J. MCQUILLIN, and ROBERT ROBINSON.

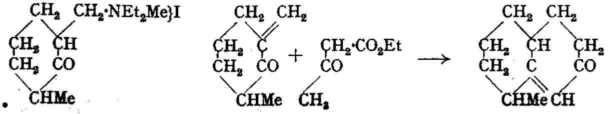
A LARGE number of experiments have been made with the object of extending the scope of the synthesis of *cyclo*hexenones described by Rapson and Robinson (J., 1935, 1285) so as to embrace the condensation of cyclic ketones with the simpler αβ-unsaturated ketones such as methyl vinyl ketone. Owing, however, to the ready polymerisation of these substances in the presence of catalysts, no direct condensation could be realised analogous to those which succeed with acetyl*cyclo*hexene or acetyl*cyclo*pentene. We therefore made trials with substances capable of ready decomposition with formation of the unsaturated ketones, hoping to take advantage in this way of the progressive liberation of the reactant in minimal concentration and at optimal reactivity. No success followed our earlier attempts to employ the β-chloroalkyl methyl ketones, but when most of the present work was completed the condensation of 2-methyl*cyclo*hexanone and methyl β-chloroethyl ketone in alcoholic solution in the presence of sodium ethoxide was found to yield (about 15—20%) *2-keto-10-methyl-*$\Delta^{1:9}$*-octalin* (I). Apart from this case we have employed quaternary ammonium salts as the source of the unsaturated ketones. The crude, uncrystallisable methiodides of bases prepared by the Mannich reaction (condensation of a keto-methylene with diethylamine hydrochloride and formaldehyde, $\cdot CO\cdot CH_2\cdot + CH_2O + NHEt_2 \longrightarrow \cdot CO\cdot CH\cdot CH_2\cdot NEt_2$) were condensed under various conditions with the sodio-derivatives of ketones or with ketones (containing $\cdot CO\cdot CH\dot{:}$) in the presence of sodium ethoxide. A typical case is that illustrated below (method A):


(I.)

The yield in this example was 35—40%. The constitution (I) attributed to the product follows from its behaviour on dehydrogenation and from the independent synthesis of the isomeride which might have been obtained if the 6-methylene group of 2-methyl*cyclo*hexanone had been implicated in the reaction.

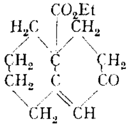
The methyloctalone (I) was not dehydrogenated on heating with palladised charcoal, and when heated with selenium it afforded β-naphthol in poor yield. Catalytic reduction of (I) afforded a crystalline *methyldecalone*.

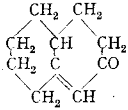
For the preparation of *2-keto-8-methyl-*$\Delta^{1:9}$*-octalin* (II), the "Mannich" base from 2-methyl*cyclo*hexanone was converted into a methiodide and then condensed with ethyl acetoacetate in alcoholic sodium ethoxide; the intermediate β-ketonic ester suffered hydrolysis under the conditions of the experiment (method B):


(II.)

The methyloctalone (II) is quite different from (I); the respective *semicarbazones* and 2 : 4-*dinitrophenylhydrazones* show depressed melting points on admixture, and when it was heated with palladised charcoal, 7-hydroxy-1-methylnaphthalene was obtained and recognised as its *p*-nitrobenzeneazo- and benzoyl derivatives. Thus, by adopting one or the other of the above devices, we can build on the new *cyclo*hexane ring in either of the alternative directions at will. In the case of *cyclo*hexanone, method A is not satisfactory because *cyclo*hexylidene*cyclo*hexanone is produced and is difficult to separate from the octalone. Accordingly ethyl *cyclo*hexanonecarboxylate is employed and the product with $Me{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}NEt_2Me\}I$ is the keto-ester (III). This is hydrolysed with formation of *2-keto-*$\Delta^{1:9}$*-octalin* (IV). Naturally method B is also available for the preparation of (IV), and this route is the better of the two; the starting materials are more readily accessible and the yield is superior.

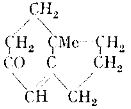
The octalone (IV) is readily dehydrogenated on heating with palladised charcoal, with formation of β-naphthol.

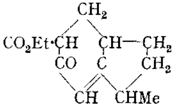
(III.) 

 (IV.)

Catalytic reduction of (IV) in neutral solution gives *cis*-β-decalone.

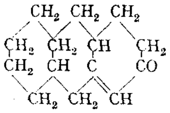
Starting with 2-methyl*cyclo*pentanone, method A gave *5-keto-8-methyl-*$\Delta^{4:9}$*-tetrahydrohydrindene* (V): method B was used for the preparation of *5-keto-6-carbethoxy-3-methyl-*$\Delta^{4:9}$*-tetrahydrohydrindene* (VI).

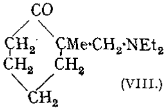
(V.) 

 (VI.)

The ketone, isomeric with (V), obtained on hydrolysis was mixed with a substance of lower carbon content, but its derivatives could be isolated in a pure condition and were quite different from those of (V).

The sodio-derivative of *trans*-β-decalone condensed with 4-diethylaminobutan-2-one methiodide (method A) with formation of *2-keto-*$\Delta^{1:13}$*-dodecahydroanthracene* (VII), the constitution of which follows from its dehydrogenation with formation of anthracene and β-anthranol.

(VII.) 

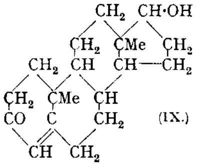
 (VIII.)

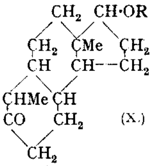
This result is in harmony with the observations of Butenandt and Wolff (*Ber.*, 1935, **68**, 2093), who show that cholestanone and coprostanone are brominated in the 2- and the 4-position respectively. Hence we anticipate that *cis*-β-decalone will be convertible by method A into a ketododecahydrophenanthrene and experiments with the object of testing this point are in progress.

In order to complete the chain of evidence for the constitution of the ketones (I) and (II), it seemed desirable to show that the "Mannich" base from 2-methyl*cyclo*hexanone is of the form assumed and not (VIII). It was accordingly successively converted into *2-methyl-6-methylene*cyclo*hexanone*, the known 2 : 6-dimethyl*cyclo*hexanone, and 2 : 6-dimethylphenol.

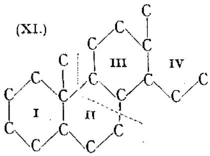
In connection with the dehydrogenation of *cyclo*hexanones we place on record a convenient method for the preparation of 2:6-dibenzylphenol from dibenzylidene*cyclo*hexanone. This transformation has been effected by Weiss and Ebert (*Monatsh.*, 1935, **65**, 399), who heated the unsaturated ketone with a mixture of acetic acid, acetic anhydride and hydrogen bromide at 52—55° for 11 hours and obtained dibenzylphenyl acetate. The isomeric change is brought about under our conditions by successive hydrogenation and dehydrogenation with or without isolation of the intermediate dibenzyl*cyclo*hexanone. 2 : 6-*Di-p-anisylphenol* was readily obtained in a similar fashion from dianisylidene*cyclo*hexanone. The methods herein described have many applications to groups other than the sterols and testicular hormones and they are particularly relevant to the sesquiterpene field; this subject is being pursued in collaboration with Professor J. L. Simonsen.

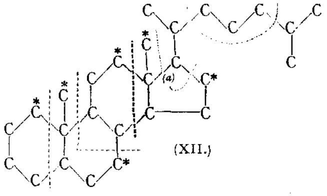
Biogenesis of the Sterols.—It is obvious that testosterone (IX) could be synthesised by an application of method A to the ketone (X) provided that the latter has the correct stereochemical constitution and that the neutral group R can be safely detached from the product.


(IX.)


(X.)

This is not surprising, because we directed our work into these channels with foreknowledge that the structures obtained would be analogous to those of the sterol group. It seemed, however, more than a mere coincidence that the same method could theoretically be used to build up the rings I, II, and III of the sterol skeleton, each stage of *cyclo*hexenone construction being followed by reduction. Starting from a methyl*cyclo*pentanone derivative (ring IV), the addition of ring III would require methyl vinyl ketone. Then ring II is added by means of ethyl vinyl ketone, and ring III with methyl vinyl ketone again. Examination of the sterol skeleton in this light shows that it may be split up into acetone residues which may be substituted in one or both of the methyl groups. It is noteworthy that rings I, II, III and part of IV involve doubling of one and the same chain (XI).

(XI.)



(XII.)

The complete dissection of the sterol skeleton into α or $\alpha\alpha'$-substituted acetones is shown in (XII), in which the asterisked carbon atoms represent the α-substituents. Thus the units are 3—1, 1—3—1, 3—1, 1—3—1, 3, 3, 3 and in ergosterol one of the side chains also is α-substituted.

The carbon to carbon link denoted (*a*) is the only one requiring a special hypothesis and it is surely remarkable that by similar reactions, analogous to our method A, the ring skeleton of the sterols can be plausibly elaborated from acetone and formaldehyde or their biological equivalents.

It appears possible that sterinoids are synthesised in the animal organism, and should

this prove to be the case a hypothesis on the lines adumbrated would doubtless be preferred to one based on the condensation of *iso*pentane units. Similarly sterols are characteristic constituents of yeasts and other fungi which do not, so far as we are aware, synthesise typical terpenoid substances with the exception of the lipochromes (cf. Reader, *Biochem. J.*, 1925, **19**, 1040).

EXPERIMENTAL.

4-Diethylaminobutan-2-one.—This substance is mentioned in a patent ("Fortschritte," **10**, 1011) and the dimethylamino-analogue was obtained by Mannich (*Arch. Pharm.*, 1917, **255**, 261). A mixture of acetone (30 c.c.), diethylamine hydrochloride (21 g.), paraformaldehyde (8·4 g.), and alcohol (5 c.c.) was refluxed for 8 hours. The base, isolated by addition of sodium hydroxide, ether extraction, and distillation, had b. p. 76—78°/15 mm., $n_D^{16°}$ 1·4628 (21 g. or 66%). On treatment with an equal weight of methyl iodide in the cold, the viscous methiodide was obtained; it could not be purified and was employed after washing with ether.

2-Keto-$\Delta^{1:9}$-octalin (IV).—The methiodide of 2-diethylaminomethyl*cyclo*hexanone, which could not be crystallised, was prepared by mixing the components below 30°; it is a white, semi-solid mass, readily soluble in alcohol and water and insoluble in ether. (A) A solution of diethylaminomethyl*cyclo*hexanone methiodide (35·5 g., 1 mol.) in a little alcohol was added to one of ethyl sodioacetoacetate (from 3·14 g. of sodium and 18 g. of the ester; 1·25 mols.) in absolute alcohol (140 c.c.) and the mixture was refluxed for 3 hours. After dilution with water the neutral product was isolated by means of ether and distilled; b. p. 95—105°/2—3 mm.; redistilled, b. p. 101—102°/2—3 mm. (8 g. or 50%), $n_D^{18°}$ 1·5238 (Found: C, 79·8; H, 9·3. $C_{10}H_{14}O$ requires C, 80·0; H, 9·3%).

(B) A solution of ethyl *cyclo*hexanone-2-carboxylate (17 g.) in alcoholic sodium ethoxide (2 g. of sodium in 150 c.c.) was cooled in ice, and diethylaminobutanone methiodide (20 g.) in alcohol (60 c.c.) gradually added. After 1 hour the solution was refluxed for 3 hours, cooled, and mixed with water and ether. After removal of the solvent from the dried ethereal layer the residue was distilled and afforded 3·2 g. of recovered ethyl *cyclo*hexanonecarboxylate, a small mixed fraction, and then 8·4 g., b. p. 179—180°/15 mm.; redistilled, b. p. 175—176°/10 mm.; $n_D^{12°}$ 1·5102 (Found: C, 69·6; H, 8·0. $C_{13}H_{18}O_3$ requires C, 70·3; H, 8·1%). The substance is slightly impure *ethyl 2-keto-$\Delta^{1:9}$-octalin-10-carboxylate* (or, much less probably, *ethyl 2-keto-$\Delta^{1:9}$-octalin-8-carboxylate*). This ester (5 g.) was hydrolysed by boiling for 8 hours with potassium hydroxide (5 g.) and water (25 c.c.), after which 0·6 g. of unchanged substance could be recovered on isolation and distillation of the oil. The lower-boiling fraction (1·1 g.), b. p. 104—105°/4 mm., $n_D^{17°}$ 1·5241, was found to be identical with the octalone obtained according to (A).

The *semicarbazone*, prepared in cold aqueous alcoholic solution in the presence of sodium acetate, crystallised from alcohol in white needles, m. p. 208° (Found: C, 69·3; H, 8·3; N, 20·3. $C_{10}H_{17}ON_3$ requires C, 63·8; H, 8·2; N, 20·3%). A mixture of specimens prepared from ketones from (A) and (B) had m. p. 208°.

The 2 : 4-*dinitrophenylhydrazone* (from A or B) crystallised from aqueous methyl alcohol, or alcohol–ethyl acetate, in scarlet plates, m. p. 168° (Found: C, 58·1; H, 5·7; N, 16·6. $C_{16}H_{18}O_4N_4$ requires C, 58·2; H, 5·5; N, 17·0%). A mixture of the derivatives prepared from (A) or (B) ketones had m. p. 167—168°.

On hydrogenation at room temperature and atmospheric pressure in the presence of palladised strontium carbonate (2%), a product, b. p. 74—76°/2 mm., $n_D^{20°}$ 1·4888, was obtained. This was found to be a β-decalone, since it gave a 2 : 4-*dinitrophenylhydrazone* crystallising from alcohol in orange needles, m. p. 155—156° (Found: C, 57·9; H, 6·2; N, 16·5. $C_{16}H_{20}O_4N_4$ requires C, 57·8; H, 6·0; N, 16·9%). A mixture with the dinitrophenylhydrazone of *trans*-β-decalone had m. p. 137°.

The semicarbazone was prepared and crystallised to constant m. p. 182—183°. Hückel (*Annalen*, 1925, **441**, 1) gives m. p. 182—183° for the semicarbazone of *cis*-β-decalone (*trans*-β-decalone semicarbazone, m. p. 192—193°). Hence the decalone obtained by reduction of the octalone is probably *cis*-β-decalone. It should be noted, however, that crude decalone containing approximately 40% of the *cis*-isomeride affords the semicarbazone, m. p. 182—183°. It is possible, therefore, that the *cis*-decalone we have obtained was mixed with some of the *trans*-isomeride.

Dehydrogenation of 2-Keto-$\Delta^{1:9}$-octalin. Formation of β-Naphthol.—The octalone (0·7 g.) was heated with palladised charcoal * (0·1 g.) for 4 hours at 330—335°, hydrogen being rapidly

* Prepared according to Ruzicka from 2 g. of palladous chloride and 11 g. of active charcoal.

evolved. The ether-soluble product was almost entirely pseudo-acidic and, on acidification of the filtered alkaline solution, crude β-naphthol (0·4 g.) was obtained. A portion crystallised from light petroleum had m. p. 120—121°, alone or mixed with authentic β-naphthol.

*2-Methyl-6-diethylaminomethyl*cyclo*hexanone*.—The yield in the preparation of this substance varies within wide limits according to the conditions, but, working in the following manner, it should be from 60—65%. A mixture of 2-methyl*cyclo*hexanone (40 g., 2 mols.), diethylamine hydrochloride (19·6 g., 1 mol.), paraformaldehyde (6·5 g., 1·2 mols.), and *cyclo*hexanol (100 g.) was heated at 110° during 2 hours. Water and ether were added, the aqueous layer (A) separated, then basified with cooling in ice, and the *base* isolated by means of ether. The product had b. p. 95—98°/3 mm., $n_D^{23°}$ 1·4642 (Found: C, 73·1; H, 11·7; N, 7·1. $C_{12}H_{23}ON$ requires C, 73·1; H, 11·7; N, 7·1%). The extremely hygroscopic methiodide was obtained from the components by interaction below 30°.

*2-Methyl-6-methylene*cyclo*hexanone*.—If the aqueous solution (A, above) is concentrated, a crude hydrochloride is obtained; this, heated under diminished pressure, decomposes with formation of the *methylene-ketone*, which is purified by distillation; b. p. 62°/9 mm., $n_D^{13°}$ 1·476 (Found: C, 76·8; H, 9·7. $C_8H_{12}O$ requires C, 77·4; H, 9·7%). The condensation *product* with 2 : 4-dinitrophenylhydrazine may be a hydrazone or a pyrazoline; it crystallised from alcohol in bright red needles, m. p. 155° (Found: C, 55·5; H, 5·4; N, 18·6. $C_{14}H_{16}O_4N_4$ requires C, 55·3; H, 5·3; N, 18·4%). The methylene-ketone was hydrogenated under 2 atmospheres pressure, palladised strontium carbonate being used as the catalyst. The product had b. p. 60°/10—11 mm., $n_D^{14°}$ 1·453 (Wallach, *Annalen*, 1913, **397**, 200, gives n_D 1·4476 for 2 : 6-dimethyl*cyclo*hexanone), indicating that reduction was not quite complete. The vapour of this ketone was slowly passed ten times over palladised charcoal at 330—335°; the product then crystallised, m. p. 47° (Found: C, 78·2; H, 8·3. Calc. for $C_8H_{10}O$: C, 78·7; H, 8·2%). Bamberger (*Ber.*, 1903, **36**, 2036) stated that 2 : 6-dimethylphenol had m. p. 49° and our substance had the characteristic odour and other properties of this xylenol.

2 : 6-Dibenzylphenol.—Borsche (*Ber.*, 1912, **45**, 50) has reduced dibenzylidene*cyclo*hexanone in alcoholic solution by means of hydrogen in the presence of colloidal palladium; he gives the m. p. 114°. We worked in dioxan solution with 5% of a nickel–kieselguhr catalyst (20% of nickel) at 100°. Rapid decolorisation occurred and the product had m. p. 119° after crystallisation from light petroleum (yield, quantitative) (Found: C, 86·3; H, 7·9. Calc. for $C_{20}H_{22}O$: C, 86·3; H, 7·9%). Dehydrogenation could not be effected by the nickel catalyst, but occurred when palladised charcoal was employed. Eventually a virtually one-stage process was evolved and the yield of dibenzylphenol was raised to 75—80%. Hence this is a preparative method of some importance and the details are the following:

Hydrogen was bubbled through a mixture of dibenzylidene*cyclo*hexanone (100 g.) and palladised charcoal (3 g.) at 200—250°, the colour being quickly discharged. The temperature was then raised to 325—330° and hydrogen was evolved during about 9 hours. The product was distilled; the fraction, b. p. 235—245°/11 mm., crystallised as a waxy mass (Weiss and Ebert, *loc. cit.*, give b. p. 238°/10 mm.; they describe the phenol as a solid but did not recrystallise it. Short, J., 1929, 553, obtained the phenol as an oil, one of the products of interaction of sodium *o*-benzylphenoxide and benzyl chloride). After redistillation it had b. p. 210°/3 mm., m. p. 30° (Found: C, 87·5; H, 6·7. Calc. for $C_{20}H_{18}O$: C, 87·6; H, 6·6%). The substance may be crystallised from light petroleum (b. p. $< 40°$), by chilling the solution, in long colourless needles, m. p. 30°. The acetyl derivative was obtained by the use of acetic anhydride and pyridine; it crystallised from aqueous acetic acid in needles, m. p. 75·2° (Weiss and Ebert, *loc. cit.*, give m. p. 74—77°) (Found: C, 83·6; H, 5·9. Calc. for $C_{22}H_{20}O_2$: C, 83·6; H, 6·3%). 2 : 6-Dibenzylphenol is cryptophenolic, being insoluble in 2*N*-sodium hydroxide, even on warming.

It is interesting to note that according to Huston, Swartout, and Wardwell (*J. Amer. Chem. Soc.*, 1930, **52**, 4484), 4-benzyl-2-methylphenol is easily soluble in 5% sodium hydroxide solution, whereas 6-benzyl-2-methylphenol is not.

4-Nitro-2 : 6-dibenzylphenol.—A mixture of nitric acid (1·2 g., *d* 1·42) and acetic acid (10 c.c.) was added to dibenzylphenol (5 g.) dissolved in acetic acid (100 c.c.) with stirring at room temperature. After 10 minutes sufficient water was added to produce a turbidity; the almost pure derivative crystallised. A less pure product is obtainable from the filtrate by addition of more water. The *substance* crystallised from 50% acetic acid in very pale yellow needles, m. p. 124° (Found: C, 75·6; H, 5·3; N, 4·2. $C_{20}H_{17}O_3N$ requires C, 75·2; H, 5·3; N, 4·4%). It is insoluble in cold aqueous sodium carbonate but, on heating, a yellow solution is produced and the undissolved crystals are coloured bright *orange-red*. On cooling and shaking with ethyl

acetate the whole of the substance passes into the organic solvent. On shaking the ethyl acetate solution with aqueous sodium hydroxide a bright *yellow* sodium salt is precipitated. This is the form that crystallises in needles from aqueous solutions containing a little sodium hydroxide; on warming, best in presence of excess of sodium hydroxide, it is transformed into the needles of the orange-red modification. The alcoholic solution of the nearly colourless nitrophenol is bright yellow and gives the yellow sodium salt on the addition of sodium hydroxide. On reduction in acid solution the very unstable dibenzyl-*p*-aminophenol was obtained and no satisfactory method for the oxidation of this to *dibenzyl-*p*-benzoquinone* was discovered. Ferric chloride gave a 5% yield of the quinone (Found: C, 83·3; H, 5·7. $C_{20}H_{16}O_2$ requires C, 83·3; H, 5·5%). The latter substance, which is readily soluble in most organic solvents, crystallises from aqueous acetic acid in yellow needles, m. p. 76—77°; its alcoholic solution becomes purple on the addition of sodium hydroxide, the colour changing through greenish-brown to reddish-brown. The solution in sulphuric acid becomes deep reddish-brown on heating and a brown solution is obtained on dilution with water; this gives a violet coloration on the addition of sodium carbonate.

The *methyl* ether of the nitrodibenzylphenol was prepared from its potassium salt, suspended in alcohol, and methyl sulphate in excess. The very pale yellow substance was crystallised from aqueous alcohol and had m. p. 70—71° (Found: C, 75·6; H, 5·7. $C_{21}H_{19}O_3N$ requires C, 75·7; H, 5·7%). After reduction of this derivative, oxidation to the quinone was found to be no easier than in the case of the aminophenol.

*2 : 6-Di-*p*-anisylphenol.*—This, obtained in 60% yield from dianisylidene*cyclo*hexanone by treatment with palladised charcoal and hydrogen as described for dibenzylphenol, crystallised from light petroleum (b. p. 60—80°) in colourless prismatic needles, m. p. 66—67° (Found: C, 79·2; H, 6·3. $C_{22}H_{22}O_3$ requires C, 79·0; H, 6·6%). Demethylation of this substance afforded resinous material, which is not surprising because the product should be a possible condensation product of 3PhOH with $2CH_2O$.

2-Keto-8-methyl-$\Delta^{1:9}$-octalin (II).—A solution of 2-methyl-6-diethylaminomethyl*cyclo*hexanone methiodide (6·9 g., 1 mol.) in a little absolute alcohol was added to one of ethyl sodioacetoacetate (from 0·52 g. of sodium and 2·9 g. of the ester; 1·1 mols.) in alcohol (25 c.c.), and the mixture refluxed for 4 hours. The *product*, worked up as in the case of the lower homologue (above), gave 2 g. (60%), b. p. 97—105°/2—3 mm.; redistilled, b. p. 102°/2—3 mm., $n_D^{20°}$ 1·5148 (Found: C, 80·3; H, 9·8. $C_{11}H_{16}O$ requires C, 80·4; H, 9·8%). The *semicarbazone* crystallised from alcohol in colourless needles, m. p. 210—211° (Found: C, 65·5; H, 8·5; N, 18·9. $C_{12}H_{19}ON_3$ requires C, 65·2; H, 8·6; N, 19·0%). The *2 : 4-dinitrophenylhydrazone* crystallised from alcohol in dark red needles, m. p. 172° (Found: C, 59·0; H, 5·8; N, 16·0. $C_{17}H_{20}O_4N_4$ requires C, 59·3; H, 5·8; N, 16·3%). Dehydrogenation by means of palladised charcoal, under the conditions already described for the conversion of octalone into β-naphthol, afforded a phenolic product that could not be crystallised. It undoubtedly consisted, however, of 7-hydroxy-1-methylnaphthalene, because it gave a *p*-nitrobenzeneazo-derivative and a benzoyl derivative tallying with the description of Vesely and Stursa (*Coll. Czech. Chem. Comm.*, 1933, **5**, 170). The former derivative crystallised from acetic acid and from nitrobenzene in red prismatic needles, m. p. 260° (Vesely and Stursa give m. p. 262°) (Found: C, 66·3; H, 4·4; N, 13·8. Calc. for $C_{17}H_{13}O_3N_3$: C, 66·4; H, 4·2; N, 13·8%). The benzoate crystallised from methyl alcohol in large, colourless prisms, m. p. 88—89° (*loc. cit.*, m. p. 88—90°).

2-Keto-10-methyl-$\Delta^{1:9}$-octalin (I).—(A) A mixture of 2-methyl*cyclo*hexanone (33 g.), powdered sodamide (6·1 g.), and dry ether (50 c.c.) was stirred for 4 hours in a stream of dry nitrogen at room temperature. A solution of 4-diethylaminobutan-2-one methiodide (43 g.) in absolute alcohol (20 c.c.) was then gradually added and after 4 hours the solution was refluxed for 2 hours. Dilute hydrochloric acid and ether were added and the ethereal solution was separated, dried, and distilled, giving 9·3 g. (38%), b. p. 143—145°/16 mm.; redistilled, b. p. 139°/15 mm., $n_D^{16°}$ 1·5341 (Found: C, 80·0; H, 9·7. $C_{11}H_{16}O$ requires C, 80·4; H, 9·8%). The *semicarbazone* crystallised from alcohol in colourless prisms, m. p. 203·5—204° (Found: C, 65·1; H, 8·7; N, 18·8. $C_{12}H_{19}ON_3$ requires C, 65·2; H, 8·6; N, 19·0%). The *2 : 4-dinitrophenylhydrazone* formed scarlet prisms from alcohol; m. p. 169° (Found: C, 59·3; H, 5·9; N, 16·1. $C_{17}H_{20}O_4N_4$ requires C, 59·3; H, 5·8; N, 16·3%). Mixtures with the isomeric derivatives of 2-keto-8-methyloctalin (above), m. p.'s 211° and 172—173° respectively, melted at 185—187° (semicarbazones) and 136—140° (dinitrophenylhydrazones).

(B) 2-Methyl*cyclo*hexanone (9·5 g., 1 mol.) was added to a solution of sodium *iso*propoxide (from 2·5 g. of sodium) in *iso*propyl alcohol (400 c.c.). (Later we found that ethyl alcohol may be employed with almost the same results.) Into the mixture, cooled below 0°, 4-chloro-

butan-2-one (10 g., 1 mol.) was introduced during ½ hour. After being kept at 0° for 18 hours, the product was worked up in the known manner and afforded 2 g., b. p. 129—133°/12 mm., $n_D^{19°}$ 1·5250. The yield was therefore about 15%, but we are engaged in efforts to develop this potentially useful variant. The semicarbazone, m. p. 204°, and the 2 : 4-dinitrophenylhydrazone, m. p. 169°, when intimately mixed with authentic specimens (prepared as under A) did not depress the respective melting points.

Dehydrogenation of 2-*Keto*-10-*methyloctalin*.—The ketone (2·9 g.) was kept at 330° for 8 hours with palladised charcoal (0·2 g.) : hydrogen was not evolved and 1·1 g. of unchanged methyloctalone could be recovered. The tarry residue was not phenolic. When, however, the ketone (1·5 g.) was heated with selenium (6 g.) at 300—315° for 4 hours and then at 330—340° for 18 hours, β-naphthol (0·2 g.) was produced, m. p. (after crystallisation from light petroleum) 120—121° alone or mixed with an authentic specimen.

2-*Keto*-10-*methyldecalin*.—2-Keto-10-methyl-$\Delta^{1:9}$-octalin (3·2 g.) in alcoholic solution absorbed 460 c.c. of hydrogen at atmospheric pressure in the presence of palladised strontium carbonate (0·3 g. of 2%). The reduction *product* had b. p. 95—96°/3 mm. and crystallised on cooling. It separated from light petroleum in rectangular prisms, m. p. 47° (Found : C, 79·7; H, 10·7. $C_{11}H_{18}O$ requires C, 79·5; H, 10·8%). The 2 : 4-*dinitrophenylhydrazone* crystallised from methyl alcohol in pale yellow needles, m. p. 152—152·5° (Found : C, 59·2; H, 6·2; N, 16·2. $C_{17}H_{22}O_4N_4$ requires C, 58·9; H, 6·3; N, 16·2%).

2-*Methyl*-5-*diethylaminomethyl*cyclo*pentanone*.—A mixture of 2-methyl*cyclo*pentanone (9·8 g.), diethylamine hydrochloride (10·8 g.), paraformaldehyde (4 g.), and alcohol (5 c.c.) was heated on the steam-bath for 4 hours. The *base* (12·3 g.) was isolated in the usual manner, b. p. 112—114°/17 mm., $n_D^{19°}$ 1·4617 (Found : C, 72·1; H, 11·3; N, 7·6. $C_{11}H_{19}ON$ requires C, 72·1; H, 11·4; N, 7·7%). The methiodide prepared from this base (25·4 g.) and methyl iodide (19·9 g.) by heating on the steam-bath for ½ hour was a viscous uncrystallisable liquid, freely soluble in alcohol and insoluble in ether.

5-*Keto*-6-*carbethoxy*-3-*methyl*-$\Delta^{4:9}$-*tetrahydrohydrindene* (VI).—Ethyl acetoacetate (18·3 g.) and 2-methyl-5-diethylaminomethyl*cyclo*pentanone (45·2 g.) were added successively to an alcoholic solution (50 c.c.) of sodium ethoxide (3·3 g. of sodium); the mixture was then refluxed for 5 hours. On working up in the known manner there were obtained 10 g. of recovered ethyl acetoacetate and 5·5 g., b. p. 140—160°/20 mm. This fraction redistilled at 120—125°/3 mm.; $n_D^{20°}$ 1·4993 (Found : C, 70·1; H, 8·1. $C_{13}H_{18}O_3$ requires C, 70·3; H, 8·1%).

Derivatives of 5-*Keto*-3-*methyl*-$\Delta^{4:9}$-*tetrahydrohydrindene*.—The hydrolysis of the foregoing ester has been carried out under a variety of conditions including the use of aqueous methyl alcoholic potash, boiling 5% hydrochloric acid, and glycerol (containing 10% of water) at 180—190° for 3 hours. The typical product had b. p. 88—90°/3 mm. and $n_D^{18°}$ 1·5045. The analytical results indicated admixture of the expected ketone, $C_{10}H_{14}O$, with $C_{10}H_{16}O_2$, probably as the result of hydration at the ethylenic linkage and consequent ring-fission. However, derivatives of the ketone $C_{10}H_{14}O$ were obtained from this material. The *semicarbazone* crystallised from ethyl alcohol in colourless, nearly rectangular prisms, m. p. 196—197° (Found : C, 63·7; H, 8·2; N, 20·2. $C_{11}H_{17}ON_3$ requires C, 63·8; H, 8·2; N, 20·3%). The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol–ethyl acetate in brick-red prisms, m. p. 159—160° (Found : C, 57·9; H, 5·7; N, 17·0. $C_{16}H_{18}O_4N_4$ requires C, 58·2; H, 5·4; N, 17·0%).

5-*Keto*-8-*methyl*-$\Delta^{4:9}$-*tetrahydrohydrindene* (V).—A mixture of 2-methyl*cyclo*pentanone (49 g.), powdered sodamide (9·8 g.), and dry ether (200 c.c.) was stirred in a stream of dry nitrogen for 3 hours; 4-diethylaminobutan-2-one methiodode (71·6 g.) was then added during 2 hours with vigorous stirring, which was continued for 4 hours. After 12 hours, water was added, the alkali neutralised, and the whole extracted with ether. After removal of the solvent from the dried extract the residue was fractionated, giving some recovered methyl*cyclo*pentanone, then 11 g., b. p. 112°/4 mm., $n_D^{22°}$ 1·4984, and 3·1 g., b. p. 150—152°/3 mm. The lower-boiling fraction was the required *product* (Found : C, 80·3; H, 9·4. $C_{10}H_{14}O$ requires C, 80·0; H, 9·3%). The *semicarbazone* crystallised from aqueous methyl alcohol in long prisms, m. p. 205° (Found : C, 63·6; H, 8·3; N, 20·2. $C_{11}H_{17}ON_3$ requires C, 63·8; H, 8·2; N, 20·3%). A mixture with the semicarbazone of 5-keto-8-methyl-$\Delta^{4:9}$-tetrahydrohydrindene melted at 182—188°. The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol–ethyl acetate in scarlet prisms, m. p. 153° (Found : C, 58·3; H, 5·5; N, 17·0. $C_{16}H_{18}O_4N_4$ requires C, 58·2; H, 5·4; N, 17·0%). A mixture with the isomeric derivative (above) had m. p. 133—136°.

2-*Keto*-$\Delta^{1:13}$-*dodecahydroanthracene* (VII).—A mixture of *trans*-β-decalone (44 g.), powdered sodamide (5·9 g.), and ether (200 c.c.) was stirred in a stream of dry nitrogen for 3 hours. 4-Diethylaminobutan-2-one methiodide (42·8 g.) was then introduced during 1 hour with ice-

cooling and vigorous stirring, which was continued for 4 hours. Next day the product was worked up as in the last example and afforded 8·7 g., b. p. 152°/3 mm., n_D^{25} 1·5224 (Found C, 82·1; H, 9·9. $C_{14}H_{20}O$ requires C, 82·4; H, 9·8%). The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol–ethyl acetate in red prisms, m. p. 197—198° (Found: C, 62·2; H, 6·4; N, 14·9. $C_{20}H_{24}O_4N_4$ requires C, 62·5; H, 6·2; N, 14·6%).

Dehydrogenation of Ketododecahydroanthracene. Formation of Anthracene and β-Anthranol.—The unsaturated ketone (1·5 g.) was heated with selenium (6 g.) for 6 hours at 290—300° and the cooled product was extracted with ether. The solution was well washed with 10% aqueous sodium hydroxide, dried, and evaporated. The residue was treated in alcoholic solution with charcoal, recovered, crystallised from light petroleum (giving 40 mg., m. p. 175—180°), and then sublimed in a vacuum. This material (20 mg.), m. p. 194—196°, was oxidised by means of chromic acid in the usual manner; the product sublimed in a vacuum, forming long, characteristic needles, m. p. 273° alone or mixed with authentic anthraquinone (m. p. 275°). The substance exhibited the anthranol reaction.

The aqueous alkaline washings (above) gave on acidification a crude phenolic substance (0·25 g.), which by repeated crystallisation from alcohol was obtained in pale brown needles, m. p. 197°, exhibiting the blue fluorescence in solution and other properties of β-anthranol (m. p. 200°).

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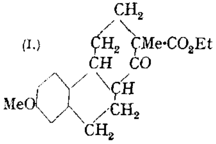
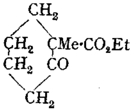
14. *Experiments on the Synthesis of Substances related to the Sterols. Part XV (Part IX continued).*

By ROBERT ROBINSON and JAMES WALKER.

ETHYL 1-keto-7-methoxy-2-methyl-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenanthrene-2-carboxylate (I), obtained by the method of Part IX (J., 1936, 752) as an oil, proves to be largely convertible into a homogeneous *semicarbazone* and thus could be safely employed as an intermediate in the projected synthesis of oestrone or a stereoisomeride. Before proceeding to further stages with such valuable material, however, we have instituted a comparison of the various methods anticipated to be available for the construction of the fourth ring.

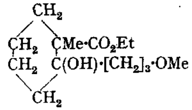
(I.) 

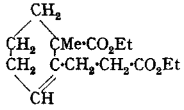
 (II.)

For this purpose we have examined the reactions of the keto-ester (II) in directions not previously investigated; the Reformatzky reaction with ethyl bromoacetate has already been studied (Chuang, Tien, and Huang, *Ber.*, 1935, **68**, 864; Linstead and Millidge, J., 1936, 480), and the condensation of (II) with ethyl cyanoacetate has been mentioned by Linstead and Millidge (*loc. cit.*; unpublished work by Linstead, Newitt, and Sapiro). (II) was readily reduced by means of aluminium *iso*propoxide (with partial transposition of alkoxy-groups), but the *sec.*-alcohol obtained could not be smoothly converted into a corresponding chloride or bromide. The subject was studied in considerable detail and a selection of typical experiments is described in the experimental section.

Reaction of (II) with ethylmagnesium iodide gave a mixture of esters undoubtedly containing the *sec.*-alcohol obtained by reduction of the ketone. The products obtained by using γ-methoxypropylmagnesium iodide could be separated except for contamination

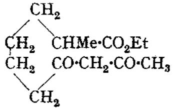
with a trace of an unsaturated compound. The main product was *ethyl* 2-*methyl*-1-γ-*methoxypropyl*cyclo*hexan*-1-*ol*-2-*carboxylate* (III), and this substance was dehydrated, and the resulting unsaturated compound catalytically hydrogenated. In the last two stages the products had the expected boiling points and other properties, but analysis disclosed the presence of impurities and further investigation of the subject is in progress. We have obtained indications of the condensation of (II) with acetylene in the presence of potassium and with ethyl β-chloropropionate and magnesium; the product of the latter reaction is probably (IV) or an isomeride with the double bond in a different position.

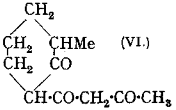
(III.) 

 (IV.)

Under the influence of sodamide, (II) condensed readily with acetone with formation of a β-*diketone*, but the additive process was unaccompanied by loss of the elements of water or of alcohol.

Evidently the acetonyl group unites with the keto-carbonyl of the keto-ester and ring-scission occurs with formation of (V). The hydrolysis of this diketone, even by means of aqueous alkalis, gives rise to the formation of 2-methyl*cyclo*hexanone. The mechanism may be in part a reversal of the original ring-fission, accompanied by loss of acetone, but it is also probable that the intermediate (VI) is produced under the appropriate conditions. When (V) was treated with boiling alcoholic sodium ethoxide, methyl*cyclo*hexanone was obtained in high yield, accompanied by a little ethyl acetoacetate.

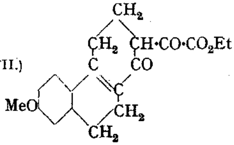
(V.) 

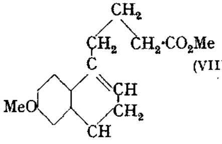
 (VI.)

We have also been engaged, and are continuously engaged, in the study of alternatives to, or improvements of, the method of preparation of the ester (I).

The least satisfactory stage is the oxidation of 7-methoxy-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenanthrol to the corresponding ketone by means of chromic acid; somewhat better results are obtained by heating the *sec.*-alcohol with cupric oxide.

Two methods designed to avoid this stage have been tried, but neither succeeded. In the first place we found that carbethoxyl cannot be introduced into the unsaturated ketone (XII) by way of the *oxalyl* derivative (VII); the latter is readily obtained, but suffers extensive decomposition on heating.

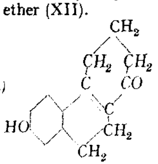
(VII.) 

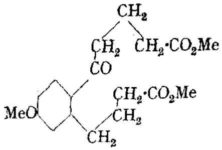
 (VIII.)

Secondly, we thought that the acid chloride corresponding to the ester (VIII) might be ring-closed and simultaneously reduced on treatment with aluminium chloride in *cyclo*-hexane solution. A general method along these lines has been disclosed by Nenitzescu and Cioränescu (*Ber.*, **1936**, **69**, 1820). The *ester* (VIII) was readily obtained by the action of sulphuric acid at −10° on methyl 5-keto-8-*m*-methoxyphenyloctoate and on hydrolysis furnished γ-6-*methoxy*-3 : 4-*dihydro*-1-*naphthylbutyric acid*, but the method of the above-mentioned authors applied to the chloride of this acid furnished no saturated ketones and

instead *1-keto-7-hydroxy*-1 : 2 : 3 : 4 : 9 : 10-*hexahydrophenanthrene* (IX) and its known methyl ether (XII).

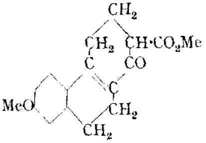
(IX.)

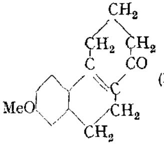




(X.)

(XI.)





(XII.)

A promising new synthetic device, which is further developed in the succeeding communication, consists in applying the Friedel–Crafts reaction to derivatives of γ-*m*-methoxyphenylbutyric acid in such a way as to introduce appropriate chains in the *p*-position to the methoxyl group. Thus methyl *m*-methoxyphenylbutyrate and γ-carbomethoxybutyryl chloride afford the *ester* (X) among the products of their interaction in the presence of aluminium chloride. Double ring-closure with the aid of potassium methoxide gives (XI), recognised as such by its ferric reaction and by hydrolysis with formation of (XII). The constitution of (XII) follows from a number of indications, the only point under consideration being the orientation of substituents in the aromatic benzene ring. The present authors (Part IX) have obtained the dehydro-derivative of the ketone as a by-product of the oxidation of its tetrahydro-compound. This ketomethoxytetrahydrophenanthrene is of known constitution (Butenandt and Schramm, *Ber.*, 1935, **68**, 2090). Furthermore, Haberland (*Ber.*, 1936, **69**, 1380), starting from β-naphthol, has synthesised a substance to which the constitution (XII) was assigned. The properties tally with those previously described by Robinson and Schlittler (J., 1935, 1288), to whose paper Haberland makes a general reference without specifically stating that the substance in question was already known.

EXPERIMENTAL.

Ethyl 1-*Keto*-7-*methoxy*-2-*methyl*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydrophenanthrene*-2-*carboxylate Semicarbazone*.—When ethyl 1-keto-7-methoxy-2-methyl-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenanthrene-2-carboxylate (J., 1936, 752) (80 mg.) was treated with semicarbazide hydrochloride (40 mg.) and crystallised sodium acetate (60 mg.) in aqueous alcoholic solution at room temperature for a few days, the *semicarbazone* (65 mg.) separated as a cream-coloured solid. Crystallisation from methyl alcohol afforded colourless, elongated, diamond-shaped prisms, m. p. 197—199° (Found : C, 64·5; H, 7·2. $C_{20}H_{27}O_4N_3$ requires C, 64·4; H, 7·2%).

Condensation of 1-*Keto*-7-*methoxy*-1 : 2 : 3 : 4 : 9 : 10-*hexahydrophenanthrene with Ethyl Oxalate*.—Freshly prepared, alcohol-free sodium ethoxide (2·3 g.) was added to a solution of 1-keto-7-methoxy-1 : 2 : 3 : 4 : 9 : 10-hexahydrophenanthrene (6·0 g.) and ethyl oxalate (4·5 g.) in dry ether (100 c.c.) and the lumps were disintegrated with a glass rod. The sodium ethoxide rapidly dissolved and an orange sodio-derivative soon separated. After the mixture had been kept for 40 hours at room temperature, ice and dilute sulphuric acid were added, orange needles then separating. These were taken up in a large volume of ether; the dried extract on evaporation gave an orange solid in practically quantitative yield. Recrystallisation from methyl alcohol afforded deep orange prisms, m. p. 90—91° (Found : C, 70·1, 69·9; H, 6·2, 6·3. $C_{19}H_{20}O_5$ requires C, 69·5; H, 6·0%). With ferric chloride in aqueous-alcoholic solution a greenish-brown coloration was produced.

The *ester* (VII) was heated at 185—195° for 4 hours and the evolution of gas which started at *ca.* 180° was still in progress at the end of that time; the appearance of the material suggested that further decomposition was taking place. The cooled product was dissolved in ether, the

solution filtered, and after removal of the solvent the residue was distilled, b. p. 170—200°/0·2 mm.; the distillate (4·9 g.) gave a ferric reaction indistinguishable from that of the starting material. The product (280 mg.) was heated with phenylhydrazine (170 mg.) on a steam-bath for 5 hours. The resulting viscous brown syrup crystallised on trituration with a little ether and the solid was collected, washed with ether, and dried. From its ready solubility it was obviously not the expected phenylpyrazolone derivative; crystallisation from ethyl alcohol gave a voluminous mass of small prisms, m. p. 162° after sintering and darkening from 159° (Found : C, 79·1; H, 6·9; N, 9·0. $C_{21}H_{22}ON_2$ requires C, 79·2; H, 6·9; N, 8·8%). Evidently the oxalyl residue had been split off completely during heating and the substance last described is the *phenylhydrazone* of 1-*keto*-7-*methoxy*-1 : 2 : 3 : 4 : 9 : 10-*hexahydrophenanthrene*.

Methyl γ-6-*Methoxy*-3 : 4-*dihydro*-1-*naphthylbutyrate* (VIII).—A solution of methyl 5-keto-8-*m*-methoxyphenyloctoate (J., 1936, 750) (16·3 g.) in concentrated sulphuric acid (70 c.c.) at −10° was kept for 4 hours and then poured on ice. The colourless oil that separated (13·2 g.) was isolated by means of ether and distilled as a faintly yellow, limpid oil (12·5 g.) at 175—178°/0·2 mm., $n_D^{17.5°}$ 1·5550 (Found : C, 73·8; H, 7·7. $C_{16}H_{20}O_3$ requires C, 73·8; H, 7·7%).

γ-6-*Methoxy*-3 : 4-*dihydro*-1-*naphthylbutyric Acid*.—The above ester (1 mol.) was refluxed for 6½ hours with 3% methyl-alcoholic potassium hydroxide (2 mols.) and the resulting crystalline acid was isolated by means of ether. Repeated crystallisation from 75% acetic acid failed to give a product with a sharp melting point, since the microcrystalline powder softened from 123°, collapsed at 129—130°, and only cleared on further heating at *ca.* 146° (Found : C, 73·3; H, 7·0. $C_{15}H_{18}O_3$ requires C, 73·2; H, 7·3%). The *substance* was freely soluble in dilute aqueous sodium carbonate and hence was not mixed with the isomeric lactone.

1-*Keto*-7-*hydroxy*-1 : 2 : 3 : 4 : 9 : 10-*hexahydrophenanthrene*.—Dry methoxydihydronaphthylbutyric acid (11·6 g.) was converted into the acid chloride in ethereal solution (100 c.c.) by the method of Carré and Libermann (*Compt. rend.*, 1934, **199**, 1422) by means of thionyl chloride (3·8 c.c.; 1 mol.) in the presence of pyridine (3·8 c.c.; 1 mol.). The chloride, after standing in a vacuum desiccator over potassium hydroxide, was dissolved in a mixture of purified *cyclo*hexane (70 c.c.) and carbon disulphide (50 c.c.), the latter being necessary owing to the insolubility of the chloride in the former solvent, and the solution was treated in the manner described by Nenitzescu and Ciorănescu (*loc. cit.*) with finely powdered aluminium chloride (13 g.). The reaction mixture was finally treated with ice and concentrated hydrochloric acid; addition of ether facilitated separation of the resulting emulsion. It was not practicable to wash the ether–carbon disulphide solution with sodium carbonate solution owing to persistent emulsions, and therefore the crude product was isolated by evaporation of the solvent, redissolved in sufficient ether to effect complete solution, and shaken with sodium carbonate solution to remove any acidic material. On evaporation of the dried ethereal solution the crude product (5·8 g.) largely crystallised. Trituration with ether removed oily material and the cream-coloured solid (0·8 g.) then crystallised from aqueous alcohol (norit) in pale yellow plates, m. p. 220—221° (Found : C, 78·6; H, 6·5. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·5%). The *substance* dissolved in caustic alkalis to yellow solutions with an intense apple-green fluorescence and its yellow solution in concentrated sulphuric acid had a bluish-green fluorescence which was not diminished on dilution with acetic acid. When the yellow, fluorescent, aqueous alcoholic caustic alkali solution of the substance was neutralised, both colour and fluorescence disappeared and returned on continuing the addition of hydrochloric acid. The substance gave no ferric reaction.

The ethereal filtrate (above) was evaporated and the product was treated with an excess of semicarbazide hydrochloride and sodium acetate crystals in aqueous alcoholic solution. The *semicarbazone* of 1-*keto*-7-*methoxy*-1 : 2 : 3 : 4 : 9 : 10-*hexahydrophenanthrene* which separated rapidly was collected and washed with a little alcohol. It was sparingly soluble in the usual solvents and separated from *n*-propyl alcohol as a microcrystalline, cream-coloured powder which showed marked phototropy, becoming bright yellow on exposed surfaces, m. p. 238—239° (decomp.) after sintering and darkening from 232° (Found : C, 67·4; H, 6·5. $C_{16}H_{19}O_2N_3$ requires C, 67·4; H, 6·7%).

Oxidation of 7-*Methoxy*-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-*octahydrophenanthrol with Copper Oxide*.—Methoxyoctahydrophenanthrol (J., 1936, 750) (12·8 g.) was heated with copper oxide (4·4 g.), added at intervals, during 20 minutes at 280—300° (metal bath) and the cooled mixture was extracted with ether. The distillate (10·9 g.) obtained on evaporation of the ether and distillation (0·2 mm.) of the crude product was treated with semicarbazide hydrochloride (6·5 g.) and sodium acetate (8·0 g.) in the usual way; the semicarbazone (cf. *loc. cit.*) (4·9 g.) rapidly separated, m. p. 225°. Unoxidised material (7·4 g.) was recovered on dilution of the mother-liquors and extraction with ether.

*Ethyl 2-Methyl*cyclo*hexan-1-ol-2-carboxylate.*—Ethyl 2-methyl*cyclo*hexanone-2-carboxylate was reduced by Ponndorf's method (*Z. angew. Chem.*, 1926, **39**, 138). Aluminium *iso*propoxide (7 g.) was added to a solution of ethyl 2-methyl*cyclo*hexanone-2-carboxylate (12 g.) in dry *iso*propyl alcohol (60 c.c.), and the mixture was slowly distilled through an 18-inch column, fresh *iso*propyl alcohol being added at intervals to compensate for the distillate. When acetone could no longer be detected by means of sodium nitroprusside in the distilling liquid (*ca.* 2 hours), the remainder of the *iso*propyl alcohol was distilled and the residue was steam-distilled until no more oily drops came over. The crude colourless oil isolated by means of ether distilled as a colourless mobile oil (11·6 g.), b. p. 118—122°/15 mm., $n_D^{14°}$ 1·4600 [Found in two different preparations: C, 64·7, 65·4, 65·1; H, 9·6, 9·6, 9·9. $C_{11}H_{20}O_3$ (*iso*propyl ester) requires C, 66·0; H, 10·0%. $C_{10}H_{18}O_3$ (ethyl ester) requires C, 64·5; H, 9·7%]. The analysis indicates that partial replacement of ethyl by *iso*propyl has taken place and this is borne out by the composition of the 3 : 5-dinitrobenzoate.

The 3 : 5-*dinitrobenzoate* of the iso*propyl ester* was obtained by the action of 3 : 5-dinitrobenzoyl chloride in slight excess on the hydroxy-ester (490 mg.) in dry pyridine (5 c.c.). The amber syrup (1047 mg.) isolated in the known manner crystallised in contact with methyl alcohol and recrystallisation from the same solvent afforded colourless plates, m.p. 92—93° [Found: C, 54·7; H, 5·7. $C_{18}H_{22}O_8N_2$ (*iso*propyl ester) requires C, 54·8; H, 5·6%. $C_{17}H_{20}O_8N_2$ (ethyl ester) requires C, 53·7; H, 5·2%].

Attempted Replacement of the Hydroxyl Group in the Foregoing Ester by Halogen.—(a) The hydroxy-ester (9·9 g.) in pyridine (7 c.c.) was added slowly to a mixture of phosphorus tribromide (1·9 c.c.) and pyridine (1 c.c.) cooled to 0°. The ester was washed in with pyridine (3 c.c.) and the mixture was left in the ice-bath for some time. Ice-water and ether were then added and the separated ethereal solution was washed several times with dilute sulphuric acid, once with sodium carbonate solution, dried, and evaporated. The crude product gave only a feeble Beilstein test for halogen and on distillation in a vacuum a colourless, halogen-free oil (4·8 g.), $n_D^{18°}$ 1·4570, distilled over a wide range, leaving a very viscous still-residue.

(b) The hydroxy-ester (9·5 g.) in pyridine (5 c.c.) was added dropwise during 15 minutes to thionyl chloride (4 c.c.; 10% excess) in chloroform (25 c.c.) with cooling in ice-water and thorough shaking. After remaining for 2 hours at 0°, the solution was warmed on the water-bath for ½ hour, sulphur dioxide and some hydrogen chloride being evolved. The mixture was then worked up in the usual way and on distillation of the crude product in a vacuum there were obtained: (i) a colourless mobile oil (3·5 g.), b. p. 90—100°/16 mm., $n_D^{17°}$ 1·4525, with pleasant "unsaturated" odour, decolorising aqueous potassium permanganate solution and bromine in chloroform; (ii) a colourless mobile oil (1·3 g.), b. p. 100—133°/16 mm., $n_D^{17°}$ 1·4562, containing a trace of halogen; (iii) a faintly yellow oil (2·0 g.), b. p. mainly above 200°/16 mm., $n_D^{17°}$ 1·465, containing halogen.

(c) The hydroxy-ester (10 g.) in light petroleum (20 c.c.) was added slowly to phosphorus pentachloride (12 g.; slight excess) under light petroleum (20 c.c.) cooled to −10°. The mixture was allowed to rise slowly to room temperature and after 30 hours ice-water was added, and the washed solution dried and evaporated. On fractional distillation of the crude product in a vacuum there were obtained: (i) a colourless pleasant-smelling mobile oil (4·8 g.), b. p. 88—95°/15 mm., $n_D^{20°}$ 1·4513 (Found: C, 70·7; H, 9·6. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·5%); the *substance* contained a trace of chlorine and from the analysis and the decolorisation of potassium permanganate and bromine in chloroform it was obviously a derived unsaturated ester; (ii) a colourless halogen-containing oil (2·6 g.), b. p. to 130°/17 mm., leaving a small decomposed still-residue.

(d) The hydroxy-ester (5 g.) in ethyl acetate (20 c.c.) was saturated with dry hydrogen bromide at 0°, and the mixture kept below room temperature for 3 days. On examination of the product there was obtained a colourless mobile oil (2·7 g.), b. p. 133—140°/20 mm., $n_D^{24°}$ 1·4470 (Found: C, 63·4; H, 9·1; Br, 0·1. $C_{12}H_{20}O_4$ requires C, 63·2; H, 8·8%); there was a considerable still-residue.

*Attempted Condensation of Ethyl 2-Methyl*cyclo*hexanone-2-carboxylate with Acetylene.*—Ethyl 2-methyl*cyclo*hexanone-2-carboxylate (23·5 g.) was added to a suspension of powdered potassium (5 g.) in benzene (*ca.* 100 c.c.). When the potassio-derivative had been formed, a brisk stream of purified acetylene was passed for 5 hours through the amber solution, which assumed a deep reddish-brown colour. On shaking with water and ether the colour was discharged to pale yellow. The separated upper layer was dried and evaporated. On a preliminary distillation of the crude product in a vacuum there was some decomposition and on further fractionation of the distillate there were obtained: (i) a slightly yellow, mobile oil (2·9 g.), b. p. to 126°/18 mm., $n_D^{20°}$ 1·4636; (ii) a colourless mobile oil (11·7 g.), b. p. 127—138°/18 mm., $n_D^{20°}$ 1·4642; a middle fraction of

(ii) was analysed (Found : C, 65·1 ; H, 8·3%) ; (iii) a faintly yellow oil (2·6 g.), b. p. to 149°/19 mm., $n_D^{20°}$ 1·451. Fraction (ii) was unsaturated to dilute potassium permanganate solution and gave a white turbidity with ammoniacal silver nitrate solution.

*Action of Ethylmagnesium Iodide on Ethyl 2-Methyl*cyclo*hexanone-2-carboxylate.*—A solution of ethylmagnesium iodide (2·5 g. of magnesium ; 17·2 g. of ethyl iodide ; 80 c.c. of ether) was added to a solution of ethyl 2-methyl*cyclo*hexanone-2-carboxylate (18·4 g.) in ether (150 c.c.) with shaking and cooling in ice-water. Next day the mixture was warmed on the water-bath for ½ hour, cooled, and treated with ice and dilute sulphuric acid. The separated ethereal solution was washed with sodium thiosulphate solution, dried, and evaporated. The crude product was further distilled in a vacuum, giving a colourless mobile oil (17·6 g.), $n_D^{17°}$ 1·4640, without fore-running at 130—140°/19 mm., mainly at 135—138°/19 mm. (Found in two different preparations : C, 65·6, 65·7 ; H, 9·7, 9·6%).

The above product (17 g.) was refluxed for 18 hours with 20% methyl-alcoholic potassium hydroxide solution (4 mols.). The mixture, added to water, was extracted thrice with ether and the acid (11·4 g.) recovered from the alkaline solution was esterified with diazomethane (from 21 g. of nitrosomethylurea). The resulting ester was fractionally distilled into four approximately equal fractions : (i) b.p. 131—135°/21 mm., $n_D^{18°}$ 1·4578 (Found : C, 65·0 ; H, 9·8%) ; (ii) b. p. 131—136°/21 mm., $n_D^{18°}$ 1·4560 ; (iii) b. p. 134—140°/21 mm., $n_D^{18°}$ 1·4512 ; (iv) b. p. 139—145°/21 mm., $n_D^{18°}$ 1·4432 (Found : C, 65·5 ; H, 9·9. $C_{11}H_{20}O_3$ requires C, 66·0 ; H, 10·0%. $C_9H_{16}O_3$ requires C, 62·8 ; H, 9·3%). The analyses suggest contamination of the desired product with a small amount of the secondary alcohol produced by the reduction of the carbonyl group of the keto-ester by the Grignard reagent (cf. Kharasch and Weinhouse, *J. Org. Chem.*, 1936, **1**, 210, for further examples of the reduction of *cyclo*hexanones by Grignard reagents).

*Ethyl 2-Methyl-1-γ-methoxypropyl*cyclo*hexan-1-ol-2-carboxylate* (III).—The Grignard reagent was prepared from γ-methoxypropyl iodide (31 g.) (Haworth and Perkin, J., 1894, **65**, 597 ; Hamonet, *Bull. Soc. chim.*, 1905, **33**, 525), magnesium (3·6 g.) activated by heating with iodine (0·9 g.), and ether (75 c.c.) and added to a stirred solution (mercury seal) of ethyl 2-methyl*cyclo*hexanone-2-carboxylate (27 g.) in ether (140 c.c.) cooled in ice-water. A vigorous reaction ensued and after being stirred for ½ hour and kept at room temperature for 15 hours, the mixture was refluxed for ½ hour, and then decomposed by the addition of dilute sulphuric acid ; the separated ethereal solution was washed with sodium thiosulphate solution, dried, and evaporated. On distillation of the crude product in a vacuum there were obtained : (i) a colourless mobile oil (11·8 g.), b. p. to 129°/14 mm., $n_D^{18°}$ 1·4528 ; (ii) a colourless, rather limpid oil (17 g. ; approx. 45%), b. p. 158—168°/13 mm., $n_D^{18°}$ 1·4660 (Found : C, 65·9 ; H, 9·9. $C_{14}H_{26}O_4$ requires C, 65·1 ; H, 10·1%). There was no significant distillate in the range 130—158°/13 mm. Fraction (i) showed unsaturation towards tetranitromethane and bromine in chloroform.

Dehydration of the Foregoing Ester with Potassium Hydrogen Sulphate.—The above ester (17 g.) was heated with potassium hydrogen sulphate at 175° for 1·25 hours and then the product was isolated by means of ether. On distillation of the crude product a colourless mobile oil (15 g.) was collected at 140—145°/15 mm., $n_D^{18°}$ 1·4691 (Found : C, 68·1 ; H, 9·8%). The foregoing treatment with potassium hydrogen sulphate was repeated and the product isolated as before was a colourless mobile oil, b. p. 140—147°/17 mm., $n_D^{16°}$ 1·4684 (Found : C, 69·0, 69·2 ; H, 9·7, 9·9. $C_{14}H_{24}O_3$ requires C, 70·0 ; H, 10·0%. $C_{13}H_{22}O_3$ requires C, 69·0 ; H, 9·7%). The *compound* instantly decolorised bromine in chloroform and developed an intense orange-yellow colour with tetranitromethane.

Catalytic Hydrogenation of the above Unsaturated Ester.—The unsaturated ester (11·3 g.) in methyl alcohol (140 c.c.) was shaken with 2% palladised strontium carbonate (11 g.) in hydrogen under an excess pressure of 3 atms. Absorption ceased when 76% of the theoretical amount of hydrogen for the saturation of one double bond had been taken up in 40 minutes. The crude product, after removal of the solvent from the filtered solution, was heated on the water-bath with 1% ethyl-alcoholic potassium hydroxide (1·1 g. ; 50% aqueous alcohol) for 2·5 hours. The mixture, diluted with water, was then extracted with ether and the extract was dried and evaporated. A small first fraction was collected up to 139°/13 mm. and then a colourless mobile oil (8·1 g.), saturated to bromine in chloroform and tetranitromethane, distilled steadily at 140—144°/13 mm., $n_D^{15°}$ 1·4587 (Found : C, 68·3 ; H, 10·7 ; OEt + OMe, 28·4, 26·6, 28·8. $C_{14}H_{26}O_3$ requires C, 69·4 ; H, 10·7 ; OEt + OMe, 31·4%. $C_{13}H_{24}O_3$ requires C, 68·4 ; H, 10·5 ; OEt + OMe, 33·3%).

The divergence in the analytical figures from the anticipated C_{14} formula is being further investigated ; the possibility of persistent contamination with some carbinol which had survived the treatment with potassium hydrogen sulphate appears to be precluded on consideration of the relevant boiling points.

*Condensation of Ethyl 2-Methyl*cyclo*hexanone-2-carboxylate with Ethyl β-Chloropropionate.*—Magnesium (2 g.) activated by Baeyer's method was placed under a mixture (1 : 1) of anisole-benzene (15 c.c.). From a dropping-funnel charged with ethyl β-chloropropionate (9 g.; slight excess) a small quantity (*ca.* 1 g.) was added to the magnesium along with a little methyl iodide (1 c.c.). Ethyl 2-methyl*cyclo*hexanone-2-carboxylate (9 g.) was then mixed with the chloro-ester in the dropping-funnel, and the mixture was added slowly to the magnesium. There was marked evidence of reaction on warming the mixture gently over a bare flame and after all the mixture of esters had been added with intermittent heating to maintain reaction, the mixture was warmed on the water-bath for ½ hour after washing in the last traces of ester mixture with mixed solvent (16 c.c.). After keeping at room temperature for 15 hours, ether and saturated aqueous ammonium chloride solution were added and the upper layer was separated, dried, and evaporated. After elimination of fore-runnings distilling up to 130°/18 mm., distillation under a pressure of 1·5 mm. indicated the presence of two fractions having b. p.'s 150—175° and *ca.* 200°. The total distillate (6·4 g.) was refluxed for 8 hours with methyl-alcoholic potassium hydroxide (3 g.; 250 c.c.), methyl alcohol was then removed by distillation, and the neutral material recovered in the usual way by means of ether. On distillation of the crude product a rather viscous yellow oil (3·2 g.) passed over at 142—152°/0·3 mm., $n_D^{10°}$ 1·4906 (Found : C, 66·8; H, 9·3. $C_{15}H_{24}O_4$ requires C, 67·1; H, 8·9%). The *substance* immediately decolorised bromine in chloroform, which fact along with the analytical figures indicated it to be the anticipated unsaturated ester.

Ethyl 7 : 9-Diketo-2-methyldecoate (V).—A mixture of ethyl 2-methyl*cyclo*hexanone-2-carboxylate (20 g.) and acetone (8 g.) was added to powdered sodamide (5 g.) stirred under dry ether (100 c.c.). Ammonia was at once evolved and heat was generated. When the initial reaction subsided, the yellow solution was refluxed for 3 hours and kept for 12 hours at room temperature. Ice and water were added and the bright yellow aqueous solution was separated and acidified. The oil was taken up in ether, and the extract dried over sodium sulphate and distilled. After removal of the solvent there were obtained 9·8 g., b. p. 140—145°/0·33 mm. (Found : C, 63·1; H, 9·3; EtO, 18·3%), and 3·3 g. of higher b. p. (Found : C, 60·5; H, 8·8; EtO, 13·2%). The latter material was far from homogeneous and was not further examined. A portion of the lower-boiling material was twice redistilled, b. p. 138—142°/0·3 mm. (Found : C, 64·2; H, 9·2; EtO, 18·3. $C_{13}H_{22}O_4$ requires C, 64·4; H, 9·1; EtO, 18·6%). This β-diketone gives a deep blood-red ferric reaction in alcoholic solution and when ferric chloride is added to an aqueous suspension the oily drops are coloured orange-red. It condenses with diaminoveratrole in acetic acid solution to a yellow copyrine derivative exhibiting green fluorescence, and with hydroxylamine it yields an *iso*oxazole derivative as a colourless oil insoluble in aqueous alkalis. It is insoluble in aqueous sodium carbonate, but dissolves readily in sodium hydroxide solution. On boiling the alkaline solution the odour of methyl*cyclo*hexanone becomes intense. The diketone (5 g.) was refluxed with anhydrous alcoholic sodium ethoxide (0·2 g. of sodium in 50 c.c.) for 2 hours, and two-thirds of the alcohol distilled. The solution was then acidified with acetic acid, diluted with water, and shaken with ether. The extract was washed with brine, concentrated, and washed several times with aqueous sodium hydroxide. The combined alkaline aqueous solutions were acidified and extracted with ether; after removal of the solvent the small oily residue had the odour and ferric reaction of ethyl acetoacetate. This identification was confirmed by the preparation of the copper derivative, green needles from benzene, m. p. 191—192°. The dried ethereal solution was distilled, giving eventually 1·7 g. of 2-methyl*cyclo*hexanone, b. p. 155—160°; semicarbazone, m. p. 194°.

*Condensation of Methyl γ-*m*-Methoxyphenylbutyrate with γ-Carbomethoxybutyryl Chloride.*—Aluminium chloride (13·4 g.; 2 mols.) was finely powdered and placed under carbon disulphide (50 c.c.) in a three-necked flask fitted with a stirrer (mercury seal), reflux condenser and dropping-funnel. A mixture of methyl γ-*m*-methoxyphenylbutyrate (10·4 g.; 1 mol.) and γ-carbomethoxybutyryl chloride (12·5 g.; 1·5 mols.) (Clutterbuck and Raper, *Biochem. J.*, 1925, **19**, 385) in carbon disulphide (30 c.c.) was added dropwise with thorough stirring. The light brown viscous complex was stirred thoroughly and a gentle evolution of hydrogen chloride took place; no external cooling was used. After 2—3 days at room temperature the carbon disulphide was decanted, and the residue treated with ice and concentrated hydrochloric acid. The resulting heavy, light yellow oil (17·4 g.), isolated by means of ether, was immediately refluxed for 3·5 hours with 10% methyl-alcoholic potassium hydroxide solution (120 c.c.). After dilution with water, acidification with hydrochloric acid, and extraction with ether, the extract was well washed with water, dried, and evaporated, leaving a viscous, light brown syrup (9·0 g.). The crude product was dissolved in 10% potassium hydroxide solution (*ca.* 3 mols.) and shaken for

6 hours with methyl sulphate (15 c.c.), and the mixture after the addition of an excess of potassium hydroxide was heated for 3 hours on the steam-bath to hydrolyse esters. The acidic material was collected in ether in the usual way and re-esterified with methyl alcohol (40 c.c.) containing concentrated sulphuric acid (1·5 c.c.) by refluxing for 7·5 hours. The crude ester (9 g.), isolated by dilution with water and extraction with ether, distilled as a viscous, light amber oil (7·6 g.), b. p. 205—210°/0·6 mm., $n_D^{15°}$ 1·5228 (Found: C, 64·5; H, 7·1. $C_{18}H_{24}O_6$ requires C, 64·3; H, 7·1%). The following experiments show that this ester is *methyl γ-[5-methoxy-2-(γ-carbomethoxybutyryl)phenyl]butyrate* (X).

Ring-closure.—The above product (4·15 g.) in benzene (40 c.c.) was refluxed with freshly-prepared alcohol-free potassium methoxide (from 1 g. of potassium) for 4 hours. After a further 12 hours at room temperature the benzene layer had become much lighter in colour and a separation of a yellowish solid had occurred; ether and dilute sulphuric acid were added and neutral and acidic material were separated in the usual way. The acidic material (1·36 g.) was set aside (see below) and the neutral material (2 g.), which gave a reddish-brown colour with ferric chloride in alcoholic solution, was refluxed with 12% hydrochloric acid (30 c.c.) for 7 hours and the product was again separated into acidic (see below) and neutral (0·5 g.) portions; the latter still gave a coloration with ferric chloride and it was therefore refluxed for 7 hours with 20% methyl-alcoholic potassium hydroxide (large excess) and, as previously, some acidic material (see below) was isolated along with a neutral brown oil (0·3 g.), which was devoid of ferric reaction and gave a copious precipitate of the 2 : 4-dinitrophenylhydrazone of 7-methoxy-1 : 2 : 3 : 4 : 9 : 10-hexahydrophenanthrone on treatment with Brady's reagent; the very dark maroon product after recrystallisation from toluene had m. p. 256°, alone or in admixture with an authentic specimen (J., 1935, 1288).

The combined acidic material referred to above was collected and refluxed with methyl alcohol (45 c.c.) containing concentrated sulphuric acid (1 c.c.) for 10 hours. The mixture was then diluted with much water and extracted with ether. The ethereal solution was washed twice with dilute sodium carbonate solution and on acidification of the alkaline washings a small amount of acidic material was precipitated; this was collected, washed and dried (68 mg.) and after two crystallisations from aqueous acetic acid the cream-coloured prisms had m. p. 228—230° (Found in a specimen dried at 100°/15 mm.: C, 71·3; H, 5·5. $C_{14}H_{12}O_2,C_2H_4O_2$ requires C, 70·6; H, 5·9%). For 7-hydroxy-1-keto-1 : 2 : 3 : 4-tetrahydrophenanthrene Butenandt and Schramm (*loc. cit.*) quote m. p. 232° and it is considered that this may be the constitution of the present by-product (for analogous demethylation with sodium ethoxide, cf. Cohen, Cook, and Hewett, J., 1935, 454).

The crude ester (2·63 g.) was distilled in a vacuum, a viscous syrup (1·7 g.) distilling largely at 180—190°/0·1 mm. with a small amount at *ca.* 200°/0·1 mm. On standing, most of the syrup crystallised, but recrystallisation was impracticable, although fine rectangular plates separated from the oil left behind on evaporation of the solvent from a solution in light petroleum. The product in dry benzene (20 c.c.) was left with molecular potassium (0·3 g.) at room temperature for 14 hours and then boiled for 1·5 hours. Alcohol was then added to the dark brown solution, which contained gelatinous material, and the benzene solution separated after addition of water was dried and evaporated, leaving a brown glass (1·5 g.) which gave a brownish-red colour with ferric chloride in alcoholic solution. An attempt to prepare a phenylpyrazolone only gave a non-crystallisable resin.

The product was refluxed with a 20% solution of sulphuric acid in acetic acid (30 c.c.); the neutral material (0·74 g.) recovered gave a fine blood-red colour in alcoholic solution with ferric chloride. After hydrolysis of the neutral material at the boiling point with 15% methyl-alcoholic potassium hydroxide (25 c.c.) for 7 hours, the recovered neutral material (0·57 g.), a viscous red syrup, still had a faint ferric reaction and gave a copious precipitate (0·78 g.) on treatment with Brady's reagent. The dark maroon crystals which separated from toluene had m. p. 256° alone or in admixture with the 2 : 4-dinitrophenylhydrazone of 1-keto-7-methoxy-1 : 2 : 3 : 4 : 9 : 10-hexahydrophenanthrene.

The authors thank the Royal Commissioners of the Exhibition of 1851 for a Senior Studentship awarded to one of them. They also thank the Royal Society for a grant and Boots Pure Drug Co. Ltd. for undertaking the preparation of methoxyphenylbutyric acid.

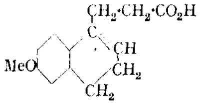
Dyson Perrins Laboratory, Oxford University. [*Received, December 14th, 1936.*]

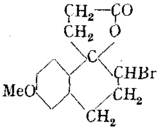
15. *Experiments on the Synthesis of Substances related to the Sterols. Part XVI.* 4-*Keto*-7-m-*methoxyphenylheptoic Acid and Some Derivatives.*

By K. H. Lin, J. Resuggan, Robert Robinson, and James Walker.

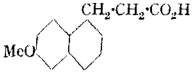
The keto-acid synthesis of G. M. and R. Robinson (J., 1925, **127**, 175; 1926, 2204; 1930, 745) gives good results in its application to the preparation of 4-*keto*-7-m-*methoxyphenylheptoic acid*, $MeO\cdot C_6H_4\cdot [CH_2]_3\cdot CO\cdot [CH_2]_2\cdot CO_2H$ (I). γ-*m*-Methoxyphenylbutyryl chloride is condensed with ethyl sodioacetylsuccinate, and the product hydrolysed with cold aqueous alcoholic potassium hydroxide and, after isolation and heating, with hot aqueous sodium hydroxide.

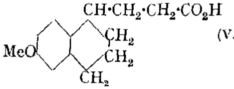
On treatment with sulphuric acid at $-10°$, the methyl ester of this acid gives β-(6-*methoxy*-3 : 4-*dihydro*-1-*naphthyl*)*propionic acid* (II) as methyl ester. The action of bromine on a solution of (II) in aqueous sodium carbonate affords a *bromo-lactone* (III), the derivatives of which will be described in a subsequent paper.

(II.) 

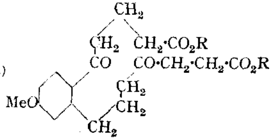
 (III.)

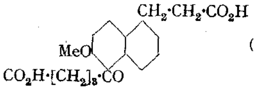
When the dihydronaphthalene derivative (II) is heated with a trace of platinum-black, it is easily dehydrogenated with formation of β-(6-*methoxy*-1-*naphthyl*)*propionic acid* (IV), a fact which establishes the constitution of (II); catalytic reduction of (II) yields the tetrahydronaphthalene derivative (V).

(IV.) 

 (V.)

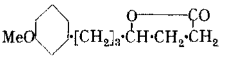
The main object of our work was to apply the Friedel–Crafts reaction to ketomethoxyphenylheptoic acid derivatives and it was hoped to couple them with the ester-chlorides of glutaric acid and α-methylglutaric acid so as to obtain substances of the type (VI);

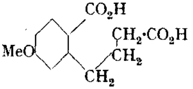
(VI.) 

 (VII.)

subsequent ring-closures with formation of near relatives of oestrone should not prove difficult. It was realised that (I) or its ester would probably be converted into a dihydronaphthalene under the influence of aluminium chloride and hence we worked at a low temperature and with an excess of the acid chloride. In this way methyl ketomethoxyphenylheptoate and γ-carbomethoxybutyryl chloride gave a reasonably good yield of condensed esters and after hydrolysis we were able to separate three crystalline acids, namely, the acid (IV), first isolated in this way, and *substances* $C_{19}H_{20}O_6$ and $C_{19}H_{24}O_6$. The compositions are those of the normal product less H_2O and minus and plus two atoms of hydrogen. Both acids are saturated to permanganate and are apparently ketonic. They are clearly naphthalene and tetrahydronaphthalene derivatives respectively and owe

their formation to disproportionation under the influence of the catalyst. It is not certain, however, that they are closely related in structure. The acid $C_{19}H_{20}O_6$ is regarded as having the structure (VII), because it was recovered unchanged after treatment for 2 hours with boiling acetic anhydride in the presence of sodium acetate. The acid $C_{19}H_{24}O_6$ is changed by this treatment and, although this does not exclude the constitution of the tetrahydro-derivative of (VII), it certainly suggests that further investigation is desirable. When methyl ketomethoxyphenylheptoate was submitted to the conditions of this experiment, but without any acid chloride, the product was a neutral oil and on hydrolysis the acids (IV) and (V) were obtained. The dihydro-acid (II) was also present in the mixtures, but in order to purify (V), (II) was destroyed by oxidation with permanganate. In order to avoid the premature formation of the naphthalene ring in an undesired manner, we reduced the keto-acid (I) to the *lactone* of *4-hydroxy-7-*m*-methoxyphenylheptoic acid* (VIII) and condensed this with *γ-carbethoxyvaleryl chloride*, $CO_2Et{\cdot}CHMe{\cdot}CH_2{\cdot}CH_2{\cdot}COCl$; the considerable fraction of b. p. compatible with the anticipated product could not be crystallised and hence no further mention of this experiment is made; the investigation will be continued employing γ-carbomethoxybutyryl chloride. The orientation of Friedel-Crafts reactions in this series is cleared up to a certain extent by the synthesis of a keto-

(VIII.) 

 (IX.)

methoxyhexahydrophenanthrene described in the foregoing communication. It is confirmed by the synthesis of *γ-(2-carboxy-5-methoxyphenyl)butyric acid* (IX) from methyl γ-*m*-methoxyphenylbutyrate and phenylethylcarbamyl chloride by treatment with aluminium chloride and hydrolysis of the product.* The constitution of (IX) follows from its conversion into the known 6-methoxytetralone, in its turn obtainable from β-naphthol by a series of processes. This investigation is being extended in several directions.

Experimental.

*4-Keto-7-*m*-methoxyphenylheptoic Acid* (I).—The process adopted was similar to that employed for the homologous acid (Part III, J., 1935, 1290; Part IX, J., 1936, 193). γ-*m*-Methoxyphenylbutyryl chloride (from 66 g. of the acid) was condensed with ethyl sodioacetosuccinate (74 g. of the ester and 8 g. of sodium) and the isolated product was shaken for 40 hours with 4·5% aqueous potassium hydroxide (3000 c.c.) and alcohol (250 c.c.). This addition of alcohol effects an improvement in the yield; also in the case of the preparation of keto-methoxyphenyloctoic acid. After this the normal process was followed and the crude mixed acids (78 g.) were esterified with diazomethane (from 78 g. of nitrosomethylurea). On distillation methyl methoxyphenylbutyrate (40 g.) and methyl ketomethoxyphenylheptoate (32 g.), b. p. 174°/0·3 mm., $n_D^{12°}$ 1·515, were obtained. The keto-ester was hydrolysed by heating with aqueous potassium hydroxide (120 c.c. of 25%) and methyl alcohol (10 c.c.), the oily acid obtained on acidification was dried in ethereal solution, and the solvent removed. It solidified on keeping and crystallised from light petroleum (b. p. 40—60°), containing a little benzene, in long, slender, colourless needles, m. p. 49—50° (Found: C, 67·2; H, 7·4. $C_{14}H_{18}O_4$ requires C, 67·2; H, 7·2%). The *semicarbazone* was readily formed and it crystallised from aqueous alcohol in colourless prisms, m. p. 117—118° (Found: C, 58·6; H, 6·9. $C_{15}H_{21}O_4N_3$ requires C, 58·6; H, 6·8%).

*Lactone of 4-Hydroxy-7-*m*-methoxyphenylheptoic Acid* (VIII).—The keto-acid was not reduced when it was treated with an excess of sodium amalgam (3%) in cold aqueous sodium hydrogen carbonate solution. A solution of 4-keto-7-*m*-methoxyphenylheptoic acid (26·5 g.) in alcohol (350 c.c.) was rapidly added to sodium (11 g.) heated in a bath at 160°. After 15 minutes, alcohol (150 c.c.) was added and after 30 minutes, when all the metal had disappeared, the alcohol was steam-distilled. A large excess of hydrochloric acid was added and next day the oil was isolated by means of ether and heated on the steam-bath for 10 minutes. The crude

* An application of a general process for the introduction of the carboxyl group embodied in patents of M. Wyler and Imperial Chemical Industries, Limited.

lactone was washed with aqueous sodium carbonate, dried in ethereal solution, and distilled; b. p. 178°/0·15 mm., $n_D^{12°}$ 1·5315 (15·5 g.) (Found: C, 72·1; H, 7·6. $C_{14}H_{18}O_3$ requires C, 71·8; H, 7·7%). Acidic material (6·5 g.) was recovered from the soda washings; this would not lactonise, nor did it form a semicarbazone and hence it was probably 7-*m*-methoxyphenylheptoic acid resulting from over-vigorous reduction.

β-(6-Methoxy-3 : 4-dihydro-1-naphthyl)propionic Acid (II).—Methyl ketomethoxyphenylheptoate (5 g.) was dissolved in concentrated sulphuric acid (25 c.c.) at − 10°; the solution was kept at this temperature for 3 hours and then poured on ice. The solid spiro-*lactone* was at once precipitated. It was collected by means of ether and obtained as a pale greenish oil (4·5 g.) which crystallised. Nearly colourless prisms, m. p. 60—61°, separated from a concentrated ethereal solution (Found: C, 73·5; H, 7·4. $C_{15}H_{18}O_3$ requires C, 73·2; H, 7·3%). The substance is insoluble in aqueous alkalis.

A mixture of the foregoing ester (4 g.) and methyl-alcoholic potassium hydroxide (60 c.c. of 12%) was boiled without condenser for ½ hour; water and hydrochloric acid were then added and the precipitate was collected and dried (3·9 g.). The substance crystallised from benzene–light petroleum and then from benzene in short colourless needles, m. p. 115° (Found: C, 72·6; H, 7·1. $C_{14}H_{16}O_3$ requires C, 72·4; H, 6·8%). On addition of bromine water to a solution of this *acid* in aqueous sodium carbonate an opaque milky liquid was produced. The *bromo-lactone* made in this way did not crystallise with facility and was probably a mixture of stereoisomerides. On keeping and stirring, the emulsion was slowly resolved, and about half of the product could be crystallised from light petroleum. The colourless needles, m. p. 100°, appeared to be homogeneous, but the analytical results were not sharp (Found: C, 53·2; H, 5·1; Br, 25·1. $C_{14}H_{15}O_3Br$ requires C, 54·7; H, 4·8; Br, 25·7%). Essentially the substance must be the bromo-lactone (III). The acid absorbed bromine very quickly in chloroform solution, and when the product was warmed with aqueous sodium acetate (perhaps not necessary) a bromo-lactone, crystallising readily from an alcoholic solution, was produced. This material was found on analysis to be a mixture of about equal parts of a mono- and a di-bromo-compound and it is evidently difficult to avoid nuclear bromination. This line of investigation is being pursued on account of the interesting synthetic possibilities it suggests.

β-(6-Methoxy-1-naphthyl)propionic Acid (IV).—This *acid*, obtained as described below, crystallises from benzene in colourless needles, m. p. 159° (Found in a specimen crystallised from light petroleum: C, 72·7; H, 6·2; MeO, 12·9. $C_{14}H_{14}O_3$ requires C, 73·1; H, 6·1; MeO, 13·4%). It retains solvent of crystallisation after drying in a vacuum and at 100° (Found: C, 74·7, 75·4; H, 6·1, 6·3%) and the benzene was recognised by Ramsden's test. It is stable to permanganate in alkaline solution, forms a very sparingly soluble bromo-derivative in warm chloroform solution, and is especially characterised by its sodium salt, which is very sparingly soluble in aqueous sodium carbonate.

A trace of platinum-black was added to about 0·5 g. of methoxydihydronaphthylpropionic acid, and the mixture carefully heated over a free flame. Hydrogen was evolved and when the evolution ceased the acid was distilled in a high vacuum. The solid distillate was converted into the sparingly soluble sodium salt, and the acid was recovered from this derivative and crystallised from benzene; m. p. 158—160°, alone or mixed with the analysed specimen.

β-(6-Methoxy-1 : 2 : 3 : 4-tetrahydro-1-naphthyl)propionic Acid (V).—Methoxydihydronaphthylpropionic acid (5 g.) was reduced in methyl-alcoholic solution (100 c.c.) by hydrogen under 2 atm. pressure and in the presence of palladised strontium carbonate (2·5 g. of 2%). 450 C.c. (theory, 480 c.c.) were absorbed in ½ hour. Evaporation of the filtered solvent afforded an oil (4·9 g.), stable to permanganate, and this gradually crystallised. The *tetrahydro-acid* crystallised from light petroleum (b. p. 40—60°) in colourless needles, m. p. 77° (Found: C, 72·1; H, 7·7. $C_{14}H_{18}O_3$ requires C, 71·8; H, 7·7%). The substance is freely soluble in most organic solvents. When the methyl ester of this acid (prepared with the help of diazomethane) was treated with γ-carbomethoxybutyryl chloride and aluminium chloride under the conditions of the experiment described below, the starting materials were largely recovered unchanged. This supports the view that the acid $C_{19}H_{24}O_6$ is not the tetrahydro-derivative of (VII).

Condensation of Methyl Ketomethoxyphenylheptoate with γ-Carbomethoxybutyryl Chloride in the Presence of Aluminium Chloride.—A mixture of the ester (10 g., 1 mol.), the acid chloride (15·5 g., 2·5 mols.), and carbon disulphide (20 c.c.) was rapidly added to powdered aluminium chloride (20 g., 4 mols.), vigorously stirred in carbon disulphide (100 c.c.) and cooled in melting ice. Stirring was continued for 3 hours and next day the carbon disulphide was decanted, ice added, and the mixture steam-distilled for a short time. The oily product (11 g.) was isolated by means of ether. It was dissolved in methyl alcohol (75 c.c.), mixed with methyl

sulphate (5 c.c.) and 5*N*-sodium hydroxide (30 c.c.), and refluxed for 1½ hours. After concentration on the steam-bath the diluted solution was acidified and the viscous acids were collected, washed with water, and dried. They were then exhaustively extracted with boiling light petroleum (b. p. 40—60°) and from this extract, colourless prismatic needles, m. p. 154—156°, separated. The acid was recrystallised from benzene, m. p. 156°, and was then freed from unsaturated impurities by means of permanganate. The recovered acid, m. p. 159°, was identified as β-(6-methoxy-1-naphthyl)propionic acid (above). On keeping, the viscous residue hardened and it was found that crystals were present; these were insoluble in methyl alcohol or acetone and the minimum of the latter solvent was used to dissolve the oil in which the solid was embedded. On recrystallisation from acetone, in which the substance was sparingly soluble, an *acid* was obtained in colourless microscopic prisms, m. p. 210° (Found: C, 66·1, 66·1; H, 5·7, 5·9; MeO, 9·5. $C_{19}H_{20}O_6$ requires C, 66·3; H, 5·8; 1MeO, 9·0%). The acetone solution was diluted with benzene and light petroleum (b. p. 40—60°); the precipitated oil, kept at 0°, gradually hardened. It was washed with ethyl acetate–light petroleum (1 : 4), then with the same solvents (1 : 2), and finally with ethyl acetate. The pale yellow solid residue crystallised from ethyl acetate–light petroleum (2 : 1) in nearly colourless, flat prisms, m. p. 144° (Found: C, 65·0, 65·3; H, 6·6, 6·9; MeO, 9·5. $C_{19}H_{24}O_6$ requires C, 65·5; H, 6·9; MeO, 8·9%). The combined mother-liquors were diluted with light petroleum, and the mixture kept in the ice-chest. On evaporation of the clear solution a considerable crop of methoxynaphthylpropionic acid was obtained, m. p. 158° after one recrystallisation; the oily residue was dissolved in a little ethyl butyrate and on keeping at 0°, crystals of the above *acid*, m. p. 144°, separated. In a similar way two further crops of this acid were obtained and the final small residue was an uncrystallisable oil. The acid $C_{19}H_{20}O_6$ is sparingly soluble in most organic solvents, but crystallises well from aqueous acetic acid. It is stable to permanganate in aqueous solution and affords a sparingly soluble semicarbazone; it also condenses with 2 : 4-dinitrophenylhydrazine. The acid $C_{19}H_{24}O_6$ is also stable to permanganate and forms a dinitrophenylhydrazone. On heating with a trace of platinum, extensive decomposition occurred and the product could not be purified. The behaviour of these acids towards acetic anhydride and sodium acetate has already been mentioned.

*Action of Aluminium Chloride on Methyl Keto-*m*-methoxyphenylheptoate.*—The keto-ester (5 g.) was added to powdered aluminium chloride (10 g.), stirred under carbon disulphide (50 c.c.) cooled in ice and water. The conditions were then identical with those of the experiment last described. The product (5 g.) was isolated in the usual manner and freed from a trace of acidic material. The mixed esters were hydrolysed by means of aqueous methyl-alcoholic sodium hydroxide on the steam-bath; the recovered acid (4·5 g.) crystallised rapidly and completely. On crystallisation from benzene, methoxynaphthylpropionic acid (2·4 g.) was obtained; this had m. p. 158° after recrystallisation, alone or mixed with the analysed specimen. The acids in the mother-liquor could not be fractionally crystallised and accordingly the unsaturated component was destroyed by addition of potassium permanganate to the solution in aqueous sodium carbonate. On acidification of the filtered solution, an oil separated and this crystallised on keeping at 0° (*ca.* 1·7 g.). The substance crystallised from light petroleum (b. p. 40—60°) in colourless needles, m. p. 76°, alone or mixed with authentic methoxytetrahydronaphthylpropionic acid.

γ-(2-Carboxy-5-methoxyphenyl)butyric Acid (IX).—A solution of phenylethylcarbamyl chloride (25·5 g., 1·5 mols.) and methyl γ-*m*-methoxyphenylbutyrate (20·8 g., 1 mol.) in carbon disulphide (50 c.c.) was added to powdered aluminium chloride (13·5 g., 1 mol.) at room temperature; a further equal quantity of aluminium chloride was then introduced. Next day the mixture was gently refluxed for 1½ hours and cooled, and the solvent decanted. The residue was washed with light petroleum, decomposed with ice and dilute hydrochloric acid, then heated on the steam-bath for 1 hour, and the oily product (35 g.) collected by means of ether. The material contained chlorine and it was refluxed for 4½ hours with potassium hydroxide (10 g.), water (20 c.c.), and methyl alcohol (60 c.c.). Methyl sulphate (10 c.c.) was added and after 40 minutes potassium hydroxide (10 g.) and water (20 c.c.) were introduced and the mixture was boiled for ¾ hour. It was then steam-distilled, and the residue acidified and isolated by means of ether. The residual oil (19·5 g.) contained nitrogen and did not crystallise; it was exhaustively extracted with boiling light petroleum and then (11 g.) hydrolysed by refluxing with acetic acid (25 c.c.) and concentrated hydrochloric acid (50 c.c.) for 7½ hours. Acetic acid was removed by steam distillation, the residue basified and steam-distilled to remove ethylaniline, and the *acid* liberated and collected (7 g.) by means of ether. On keeping a solution in benzene, a crop of prismatic crystals separated and these were recrystallised from ethyl acetate

and then from benzene–light petroleum, forming colourless prismatic needles, m. p. 173° after sintering at 165° (Found: C, 60·5; H, 6·0. $C_{12}H_{14}O_5$ requires C, 60·5; H, 5·9%). The acid was sparingly soluble in cold water and crystallised from water in colourless needles. It was boiled with an excess of acetic anhydride for 20 minutes, and the solution then distilled, finally in a high vacuum. When all the acetic anhydride had been removed, the residue evolved gas and, without significant loss, distilled as a pale yellow oil. This crystallised at once on cooling and after recrystallisation from aqueous alcohol was obtained in colourless plates, m. p. 81° alone or mixed with authentic 6-methoxytetralone. There were indications of the presence of an isomeric acid, but it could not be separated from the viscous substances in the mother-liquor. These still contained nitrogen, so the hydrolysis was incomplete. It is certain that the main product was the phenylethylamide of the acid described above, but owing to the difficulty of the separations any estimate of the yield would be valueless.

γ-Carbethoxyvaleryl Chloride.—Ethyl γ-cyano-α-methylbutyrate is conveniently obtained by the following modification of the method of Holmes, Thorpe, and Udall (J., 1900, **77**, 947). Ethyl cyanoacetate (133 g.) was added to alcoholic sodium ethoxide (27 g. of sodium in 400 c.c.), the solution cooled, and ethyl α-methylacrylate (135 g.) added in one portion. Heat was generated and the sodio-derivative dissolved. After 2½ hours, without heating or cooling, water (50 c.c.) was added and next day the solvent was distilled. When 300 c.c. had passed over, water (150 c.c.) was added, then 100 c.c. were distilled, and water (150 c.c.) was added; finally 250 c.c. were collected. The residue was acidified and exhaustively extracted with ether. The extract was dried over sodium sulphate and distilled, finally from a bath at 200° under 15 mm. pressure. The fraction up to 150° was collected and redistilled, b. p. 175—180°/140 mm. (87 g.). The residue afforded α-methylglutaric acid on hydrolysis with boiling 50% sulphuric acid. The hydrolysis of the nitrile ester was effected as follows. Concentrated sulphuric acid (30 c.c.) was very slowly added drop by drop to ethyl γ-cyano-α-methylbutyrate (15 c.c., 14·65 g.) cooled to − 10° and mechanically stirred. The mixture became very viscous and towards the end of the operation was stirred with difficulty; addition of the last portions of sulphuric acid again reduced the viscosity. After 10 minutes (keeping below 0°) the temperature was allowed to rise to that of the room for 20 minutes. The mixture was then cooled to − 10° and crushed ice (40 g.) was slowly added; the temperature did not rise above 5°. Arrangements were made to collect the evolved gas and aqueous sodium nitrite (65 c.c. of 30%) was gradually added with shaking. 3000 C.c. of gas were collected (of which only 2240 c.c. should theoretically be nitrogen). The reaction mixture was kept at 0° for 1½ hours, then saturated with sodium sulphate, and thrice extracted with chloroform (100 c.c. each time). The chloroform extract was washed with a little saturated sodium sulphate, dried, and distilled. The residue (13·1 g.) after removal of the solvent was fractionally distilled as follows: b. p. 85—109°/0·39 mm. (1·15 g.), b. p. 109—122°/0·33 mm. (6·6 g.) (Found: C, 54·9; H, 8·2. $C_8H_{14}O_4$ requires C, 55·1; H, 8·0%) (93·5% pure on titration with 0·1*N*-sodium hydroxide), b. p. 116·5—128°/0·23 mm. (3·55 g.). In another preparation the cyano-ester (29·3 g.) gave the acid ester (27·3 g. or 83%), b. p. 116—149°/0·4—0·7 mm.

The acid ester (53·1 g.) was mixed with purified thionyl chloride (65·2 c.c.) below 0° and after some time the mixture was refluxed for ½ hour. The product was fractionated: b. p. 17·5—80°/27—40 mm. (70·1 g.); b. p. 134—142°/15—16 mm. (48·8 g.). The first fraction on redistillation gave a further 2 g., b. p. 131—137°/17 mm. (yield, 86·4%). The substance was characterised by conversion into a β-naphthylamide, the anilide and *p*-toluidide being found unsuitable for the purpose.

The acid chloride was added to an ethereal solution of β-naphthylamine and *γ-carbethoxy-valero-β-naphthylamide*, β-$C_{10}H_7$·NH·CO·CH_2·CH_2·CHMe·CO_2Et, was isolated in the known manner and crystallised from 50% alcohol (Found: C, 72·4; H, 7·2; N, 4·9. $C_{18}H_{21}O_3N$ requires C, 72·2; H, 7·0; N, 4·7%). The substance was sparingly soluble in light petroleum (b. p. 60—80°) and crystallised therefrom in colourless needles, m. p. 76·5—77·5°.

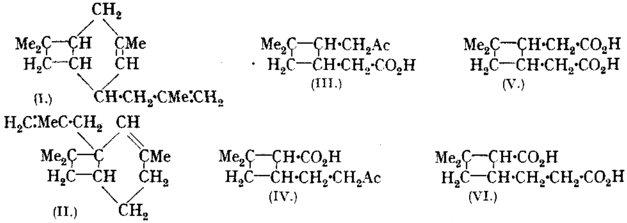
The authors thank the Government Grants Committee of the Royal Society, Imperial Chemical Industries, Limited, and Boots Pure Drug Co. for grants or for material and they also gratefully acknowledge the award by the Royal Commissioners of the Exhibition of 1851 of a Senior Studentship to one of them.

DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, December 14th*, 1936.]

16. *The Caryophyllenes. Part V. The Structure of Homocaryophyllenic Acid.*

By G. R. Ramage and J. L. Simonsen.

It was pointed out (J., 1935, 1583) that the determination of the structure of the keto-acid $C_{11}H_{18}O_3$ (Semmler and Mayer, *Ber.*, 1911, **44**, 3662) would enable a distinction to be drawn between the formulæ (I) (Ruzicka, *J. Soc. Chem. Ind.*, 1935, **54**, 509) and (II) (Ramage and Simonsen, *loc. cit.*, p. 1581) suggested for β-caryophyllene, since the former would give on oxidation the keto-acid (III), and the latter, (IV), which with sodium hypobromite would yield the homocaryophyllenic acids (V) and (VI) respectively.

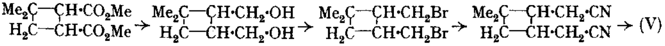


(I.) (II.) (III.) (IV.) (V.) (VI.)

Utilising *cis*-norcaryophyllenic and caryophyllenic acids, we have undertaken the synthesis of the dibasic acids, 2-carboxymethyl-1 : 1-dimethyl*cyclo*butane-3-acetic acid (V) and 2-carboxy-1 : 1-dimethyl*cyclo*butane-3-β-propionic acid (VI), in order to compare their dianilides with the dianilide, m. p. 179—180°, prepared from homocaryophyllenic acid (J., 1936, 742).

The considerable quantities of the caryophyllenic acids required for these syntheses were obtained by the direct oxidation of the caryophyllenes with nitric acid and we now find the crude acids, isolated as described in Part I (J., 1934, 1806), to be mixtures of the *cis*- and *trans*-forms, complete purification by crystallisation yielding finally the *trans*-acids. By analogy with the dianilides of *cis*- and *trans*-caryophyllenic acids, we assign to the homocaryophyllenic dianilide, m. p. 179—180°, described previously the *cis*-configuration. A repetition of the preparation of homocaryophyllenic acid, a specimen of the keto-acid regenerated from the semicarbazone, once recrystallised, being used, gave a small quantity of a second, trans-*dianilide*, m. p. 282°.

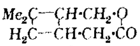
Methyl *d-cis*-norcaryophyllenate was converted by the stages outlined below into the methyl ester of (V). Owing to the poor yields and in view of the previous difficulties



encountered in the preparation of glycols and bromides of this type (Bradfield, Jones, and Simonsen, J., 1936, 1136), no attempt was made to purify the intermediate products. The *methyl* ester was faintly optically active, but analysis showed it to be not quite pure. Preparation of the crystalline dianilide indicated that a partial conversion of this *cis*- into the *trans*-configuration had occurred, since two *dianilides*, m. p. 170° and 280°, were obtained. The former was optically inactive in chloroform solution. The latter did not depress the melting point of the *trans*-dianilide of homocaryophyllenic acid, but this cannot be regarded as a proof of identity, since no depression results in admixture with the *trans*-dianilide of caryophyllenic acid. It is probable that the racemisation of methyl *d-cis*-norcaryophyllenate occurs during the reduction to the glycol, which, if it proceeds through the di-enolic form of the ester, must result in the loss of optical activity.

The *methyl* ester of (VI) was prepared by the reduction with sodium and alcohol of caryophyllenic anhydride, the resulting lactone being converted into the dibasic acid by

Blanc's method. Although the reduction of the anhydride (VII) can result theoretically in the formation of the two isomeric lactones (VIII) and (IX), a consideration of previous work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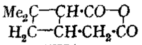
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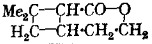

(VIII.)

on the reduction of the anhydrides of unsymmetrical acids (*inter al.*, Blanc, *Bull. Soc. chim.*, 1905, **33**, 879) suggests that (VIII) would form the main, if not the sole product. Reduction to (IX) would probably be accompanied by ring fission, as was observed in the case of sodium methyl caronate (Hariharan, Menon, and Simonsen, J., 1928, 438). This view receives support from the fact that the yield of the lactone is very poor and little unchanged caryophyllenic acid can be recovered.

The *dianilide*, prepared from the methyl ester of the acid, was optically active and melted at 206°; another specimen prepared in small quantity in a preliminary experiment melted at 212°. The slight difference in melting point may be due to a difference in optical purity, but the higher-melting anilide was insufficient in quantity for its rotatory power to be determined. There was no evidence of the presence of a *trans*-modification of the dianilide.

Whilst the racemisation which occurred in the synthesis of 2-carboxymethyl-1 : 1-dimethyl*cyclo*butane-3-acetic acid has precluded a rigid proof of its identity with homocaryophyllenic acid, we consider the dianilide, m. p. 179–180°, prepared from the latter acid to be the lævorotatory form (not necessarily optically pure) of the synthetic dianilide, m. p. 170°, and this view, in our opinion, receives support from the fact that each of these dianilides is accompanied by a higher-melting *trans*-dianilide. The difficulty involved in the preparation of the synthetic acid makes it improbable that it will be available in quantity sufficient for its resolution.

We referred previously (*loc. cit.*, p. 742) to the suggestion made by Treibs (*Ber.*, 1936, **69**, 41) that methyl betulolate was identical with methyl homocaryophyllenate. By the kindness of Dr. Treibs we have now had the opportunity of preparing the dianilide of his acid. Like homocaryophyllenic acid, it yields two dianilides, m. p. 180° and 279°, identical in all respects with the dianilides of this acid. Details of this work will be published by Dr. Treibs.

An attempt was made to utilise *X*-ray powder photographs to compare the synthetic dianilides with those derived from homocaryophyllenic and betulolic acids. We are much indebted to Professor E. A. Owen, Sc.D., and Mr. I. G. Edmunds, B.Sc., for carrying out this work. The identity of the dianilides of homocaryophyllenic and betulolic acids was confirmed and they differed from the dianilides of the two synthetic acids. Since the dianilides of the degradation acids were both optically active, identity with the dianilide of the optically inactive synthetic acid would not be expected.

These experiments lead us to conclude that, assuming caryophyllenic acid has been correctly formulated (synthetic proof of which has not yet been obtained), Ruzicka's formula (I) provides, so far as the present evidence goes, the most satisfactory representation of β-caryophyllene.

EXPERIMENTAL.

Nitric Acid Oxidation of Caryophyllene.—Caryophyllene (30 c.c.) and nitric acid (100 c.c.; *d* 1·14) were gently heated on the water-bath for 36 hours, a further quantity of acid (300 c.c.) being added at intervals. The mixture was concentrated on the water-bath, and the residual gummy acid freed from water and esterified with methyl-alcoholic sulphuric acid in the presence of benzene. In all, 3000 g. of caryophyllene were oxidised and the ester on fractionating (4 times) with a short column gave (i) b. p. up to 105°/18 mm., chiefly methyl dimethylsuccinate (250 g.), (ii) b. p. 108–116°/18 mm., methyl norcaryophyllenate (106 g.), and (iii) b. p. 122–132°/18 mm., methyl caryophyllenate (150 g.).

Methyl cis-*Norcaryophyllenate.*—The fraction (ii) was hydrolysed, and crude norcaryophyllenic acid (45 g.), m. p. 120°, isolated. A portion (12 g.) was gently refluxed with acetyl chloride: the anhydride (6 g.), b. p. 138–139°/15 mm., solidified almost completely. The remainder of the acid (33 g.) was treated with acetic anhydride at 220° for 6 hours and gave the anhydride (25 g.), b. p. 139–142°/15 mm. The combined anhydrides were refluxed with methyl alcohol (100 c.c.), benzene (100 c.c.), and sulphuric acid (25 c.c.) for 9 hours, and the ester (31 g.) purified by distillation, b. p. 117–120°/16 mm.

Methyl dl-2-*Carbomethoxymethyl*-1 : 1-*dimethyl*cyclo*butane*-3-*acetate*.—The above ester (10 g.) in ethyl alcohol (150 c.c., distilled over sodium) was poured on clean sodium (20 g.) and when the vigorous reaction had subsided the mixture was heated at 130° until the sodium dissolved. The cooled solution was acidified with concentrated hydrochloric acid, with the addition of sufficient water to dissolve the sodium chloride, and extracted repeatedly with chloroform. Removal of the solvent left a mobile oil (3 g.), which was gently heated with phosphorus tribromide (5 g.) on the water-bath for 1 hour. Ice was added, the precipitated oil collected in ether, the ethereal extract shaken with sodium carbonate solution and dried, and the ether evaporated. The liquid *dibromo*-compound (3·2 g.), after keeping in a vacuum, was reasonably pure (Found : Br, 52·5. $C_8H_{14}Br_2$ requires Br, 59·3%). It was refluxed with methyl alcohol (20 c.c.) and finely powdered potassium cyanide (2·0 g.) for 18 hours and the resulting nitrile, isolated with ether, was heated for 3 hours with methyl-alcoholic hydrogen chloride (20 c.c.). Ammonium chloride separated from the cooled solution, water was added, and the *methyl* ester after extraction with ether was distilled, b. p. 140–160°/20 mm. (1·7 g.). The ester obtained from three such experiments, on refractionation, gave an oil (3·5 g.), b. p. 145–155°/19 mm., $n_D^{20°}$ 1·4480, α_{5461} + 0·56°, which was not quite pure (Found : C, 61·4 ; H, 9·3. $C_{12}H_{20}O_4$ requires C, 63·2 ; H, 8·8%).

The dianilide was prepared by Hardy's method (J., 1936, 398). To a Grignard solution prepared from magnesium (0·5 g.) and ethyl bromide (2·5 g.), aniline (2·0 g.) was added, followed by the methyl ester (1 g.) in ether (10 c.c.), and the mixture was gently refluxed. Excess of dilute hydrochloric acid was added and after shaking the mixture was allowed to stand. The trans-*dianilide* (0·2 g.), which was insoluble in ether, separated and was collected. It crystallised from *cyclo*hexanone in long colourless needles, m. p. 280° (Found : C, 75·4 ; H, 7·4. $C_{22}H_{26}O_2N_2$ requires C, 75·4 ; H, 7·4%). The ether, from which this dianilide had separated, was dried and yielded on evaporation an oil (1 g.), which partly crystallised when mixed with dilute alcohol. Recrystallised from this solvent, the cis-*dianilide* (0·3 g.) separated in long needles, m. p. 170° (Found : C, 75·3 ; H, 7·5%).

Methyl 2-*Carbomethoxy*-1 : 1-*dimethyl*cyclo*butane*-3-β-*propionate*.—The crude methyl caryophyllenate (150 g.) (see above) was hydrolysed, and the acid (90 g.) recovered from the insoluble potassium salt. After treatment with acetyl chloride the anhydride (35 g.) was distilled, and the residual *trans*-acid converted into the anhydride by treatment with acetic anhydride at 220°. The combined caryophyllenic anhydride was fractionated, b. p. 165–172°/20 mm. (54 g.).

The anhydride (10 g.) in alcohol (100 c.c., distilled from sodium) was added to clean sodium (15 g.) and finally heated at 130° to complete the reduction. Water was added, the alcohol removed in steam, and the residue, after being strongly acidified with hydrochloric acid, distilled in steam. The distillate (1000 c.c.), saturated with salt, was repeatedly extracted with ether, and the total product (8·5 g.) from caryophyllenic anhydride (44 g.) was distilled, b. p. 142—146°/20 mm., $n_D^{20°}$ 1·4728, α_{5461} + 40·3°.

The lactone (8·2 g.) was heated with powdered potassium cyanide (5 g., dried at 250° under reduced pressure) for 6 hours at 250°, water added, and the filtered solution acidified and extracted with ether. The cyano-acid remaining after removal of the solvent was esterified with methyl-alcoholic hydrogen chloride (40 c.c.) and the *methyl* ester (5·5 g.), b. p. 145–150°/18 mm., isolated. The analysed sample had b.p. 145–146°/18 mm., $n_D^{20°}$ 1·4502, α_{5461} –4·8° (Found: C, 63·1 ; H, 9·1. $C_{12}H_{20}O_4$ requires C, 63·2 ; H, 8·8%). The *dianilide*, prepared as described above (0·7 g. from the ester, 1 g.), crystallised from alcohol (80%) in long thin plates, m. p. 206°, $[\alpha]_{5461}$ –28·3° in pyridine (*c*, 3·217) (Found : C, 75·1 ; H, 7·7%).

d-*Homocaryophyllenic Acid*.—The semicarbazone (6 g.) of the keto-acid was converted into homocaryophyllenic acid as previously described (*loc. cit.*, p. 742), and the latter esterified with diazomethane giving *methyl homocaryophyllenate* (3·5 g.), b. p. 144–150°/18 mm. The analysed fraction had b. p. 145–147°/18 mm., $n_D^{20°}$ 1·4492, $[\alpha]_{5461}$ + 56·9° (Found : C, 62·9 ; H, 8·8. $C_{12}H_{20}O_4$ requires C, 63·2 ; H, 8·8%). The ester (1 g.) was converted into the dianilide as described ; the small quantity of product, insoluble in ether, crystallised from *cyclo*hexanone in small colourless needles, m. p. 282° (Found : C, 75·4 ; H, 7·4%). From the product soluble in ether, the *cis*-dianilide (0·8 g.), m. p. 179°, $[\alpha]_{5461}$ –57·5°, in chloroform (*c* 3·360), was obtained ; it crystallised readily from alcohol (60%) in shining plates.

We are indebted to the Government Grants Committee of the Royal Society, the Chemical Society, and Imperial Chemical Industries Ltd. for grants.

The University College of North Wales, Bangor. [*Received, November 4th, 1936.*]

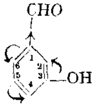
17. *The Iodination of 3-Hydroxy- and of Nitrated 3-Hydroxybenzaldehydes, and the Nitration of Certain Iodo-3-hydroxybenzaldehydes*

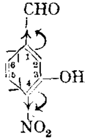
By Herbert H. Hodgson and Ernest W. Smith.

Henry and Sharp (J., 1922, **121**, 1059; 1924, **125**, 1049) found that, whereas *o*- and *p*-hydroxybenzaldehydes were dimercurated readily, the mercuration of *m*-hydroxybenzaldehyde occurred at position 2 only. Similarly Hodgson and Beard (J., 1926, 147; Hodgson E.P. 258,060) found that chlorination took place initially at position 2, but subsequent reaction occurred mainly at position 6 with, however, some reactivity at position 4. On the other hand regulated bromination was found by Hodgson and Beard (J., 1925, **127**, 876) to proceed in the positional sequence 6, 4, 2, thereby following the order of nitration (Pschorr, *Annalen*, 1912, **391**, 33). The main nitration of 3-methoxybenzaldehyde, however, takes place at position 2 with but little nitration at position 6 and none at position 4. Further, it was found (Hodgson and Beard, J., 1927, 2375) that, whereas the continued nitration of 6-nitro-3-hydroxybenzaldehyde gave a mixture of 2 : 6- and 4 : 6-dinitro-3-hydroxybenzaldehydes, the 2-nitro- and 4-nitro-3-hydroxybenzaldehydes were nitrated the second time at position 6 only.

It would be anticipated, therefore, that for the feebly kationoid reagent iodine, mono-iodination of *m*-hydroxybenzaldehyde in sodium acetate solution might occur exclusively at either the 2- or the 6- position, and probably at the latter position by analogy with the behaviour of bromine. The Kekulé formula being assumed for 3-hydroxybenzaldehyde, the above reactions all indicate a configuration (I), *i.e.*, one showing preferential reactivity for mono-substitution in the sequence 2, 6, 4. It was found that, accompanied by a very small amount of tri-iodination (*cf.* exclusive trichlorination and tribromination of *m*-hydroxybenzaldehyde in aqueous media; Hodgson and Beard, *loc. cit.*), mono-iodination occurred exclusively in position 6, and that di-iodination subsequently ensued at position 2. The constitution of the *6-iodo-3-hydroxybenzaldehyde* was confirmed by its oxidation to 6-iodo-3-hydroxybenzoic acid (Limpricht, *Annalen*, 1891, **263**, 234), and that of the 2 : 6-*di-iodo-3-hydroxybenzaldehyde* by its nitration, under conditions designed to prevent migrations, to 2 : 6-di-iodo-4-nitro-3-hydroxybenzaldehyde (Henry and Sharp, *loc. cit.*).

(I.)





(II.)

4-Nitro-3-hydroxybenzaldehyde resisted iodination under the simple conditions employed for the 6- and the 2-nitro-isomeride, which were di-iodinated to give 2 : 4-di-iodo-6-nitro- and 4 : 6-di-iodo-2-nitro-3-hydroxybenzaldehyde respectively; it was established, however, that 4-nitro-3-hydroxybenzaldehyde was oxidised and not iodinated by iodine to give 4-nitro-3-hydroxybenzoic acid. This anomalous behaviour of 4-nitro-3-hydroxybenzaldehyde is explicable, however, on the assumption that owing to the influence of the 4-nitro-group the Kekulé formula (II) for 4-nitro-3-hydroxybenzaldehyde indicates that position 2 is no longer activated by the phenolic group, while position 6 has its anionoid activity very considerably reduced by the superposed effects of the kationoid aldehyde and nitro-groups.

When 4 : 6-di-iodo-2-nitro-3-hydroxybenzaldehyde is nitrated, it is the 4-iodine which is displaced by the nitro-group to give 6-iodo-2 : 4-dinitro-3-hydroxybenzaldehyde, whereas the analogous nitration of 4 : 6-dibromo-2-nitro-3-hydroxybenzaldehyde afforded 4-bromo-2 : 6-dinitro-3-hydroxybenzaldehyde (Hodgson and Smith, J., 1931, **1500**). This apparently anomalous reaction must be ascribed to the relatively feeble negative ($-I$) inductive effect and pronounced electromeric ($+T$) effect of the iodine atom; in consequence, the di-iodo-compound will be less ionised than its dibromo-analogue, and this fact has

apparently resulted in an insufficient anionoid activity of the 6-carbon atom for reaction to be directed there; nitric acid therefore attacks the more intensely but less frequently activated 4-position.

Intense blue colours are given with alcoholic potassium hydroxide by the *p*-nitrophenylhydrazones of the aldehydes in which a nitro-group occupies the para-position in the aldehyde nucleus, the generalisation of Chattaway and Clemo (J., 1923, **123**, 3043) being thereby supported and a double quinonoid structure indicated (cf. Hodgson and Beard, J., 1927, 2375). All the *p*-nitrophenylhydrazones described below give yellow or orange colours with concentrated sulphuric acid.

EXPERIMENTAL.

Mono-iodination of m-*Hydroxybenzaldehyde*.—The aldehyde (5 g.), dissolved in hot water (500 c.c.), was treated successively with iodine (10 g.) and sodium acetate (15 g.); the mixture was heated on the water-bath until the iodine had disappeared, and then boiled. The crystalline precipitate obtained from the filtered cooled liquid was fractionally recrystallised from hot water; the first small fraction and the final fractions were the tri-iodinated compound and unchanged *m*-hydroxybenzaldehyde respectively; the middle fractions were *6-iodo-3-hydroxybenzaldehyde*, which crystallised from water in colourless needles, m. p. 130° (Found: I, 51·0. $C_7H_5O_2I$ requires I, 51·2%), and was oxidised by cold alkaline potassium permanganate to 6-iodo-3-hydroxybenzoic acid, m. p. 196° (Found: I, 47·9. Calc. for $C_7H_5O_3I$: I, 48·1%). The aldehyde formed a p-*nitrophenylhydrazone*, which crystallised from glacial acetic acid in orange needles, m. p. 215° (Found: N, 11·2; I, 33·0. $C_{13}H_{10}O_3N_3I$ requires N, 11·0; I, 33·2%).

Di-iodination of m-*Hydroxybenzaldehyde*.—A well-stirred solution of the aldehyde (2 g.) in water (100 c.c.) to which saturated aqueous sodium carbonate (30 c.c.) had been added was gradually treated with iodine (7 g.) during 30 minutes. When the iodine had disappeared, solid anhydrous sodium carbonate was stirred into the solution until precipitation ceased; the mixture of sodium salts which separated was then dissolved in water and treated with carbon dioxide. The precipitated 2 : 4 : 6-tri-iodo-3-hydroxybenzaldehyde (see below) was removed; the filtrate on acidification with hydrochloric acid gave 2 : *6-di-iodo-3-hydroxybenzaldehyde*, m. p. 144° (Found: I, 67·8. $C_7H_4O_2I_2$ requires I, 67·9%). Treatment with methyl sulphate in 10% aqueous sodium hydroxide gave 2 : *6-di-iodo-3-methoxybenzaldehyde*, m. p. 81° (Found: I, 65·2. $C_8H_6O_2I_2$ requires I, 65·4%). Both compounds crystallised from 80% aqueous alcohol in iridescent white needles.

Tri-iodination of m-*Hydroxybenzaldehyde*.—A well-stirred solution of the aldehyde (1 g.) in water (100 c.c.) and saturated aqueous sodium carbonate (30 c.c.) was treated with iodine (7 g.) and kept agitated until the iodine had disappeared. The white *sodium* salt of 2 : 4 : 6-tri-iodo-3-hydroxybenzaldehyde which separated (Found: Na, 4·4. $C_7H_2O_2I_3Na$ requires Na, 4·4%) was filtered off and redissolved in water, and 2 : 4 : *6-tri-iodo-3-hydroxybenzaldehyde* (3·5 g.) precipitated by carbon dioxide. It crystallised from alcohol in stellate clusters of pale cream needles, m. p. 146° (Found: I, 76·0. $C_7H_3O_2I_3$ requires I, 76·2%), identical with the tri-iodo-compounds mentioned above. Methylation afforded 2 : 4 : *6-tri-iodo-3-methoxybenzaldehyde*, which crystallised from alcohol in iridescent white needles, m. p. 162° (Found: I, 74·0. $C_8H_5O_2I_3$ requires I, 74·1%). The p-*nitrophenylhydrazone* of the tri-iodohydroxybenzaldehyde crystallised from glacial acetic acid in pale orange needles, m. p. 237° (decomp.) (Found: I, 59·8. $C_{13}H_8O_3N_3I_3$ requires I, 60·0%).

Improved Preparation of 2-Nitro-3-hydroxybenzaldehyde.—Pschorr's method of nitrating 100 g. of 3-hydroxybenzaldehyde (*Annalen*, 1912, **391**, 23; see also Friedländer, *Ber.*, 1914, **47**, 3040) as modified by Hodgson and Beard (J., 1925, **127**, 875) afforded only 5 g. of 2-nitro-3-hydroxybenzaldehyde, but the yield and purity of the product have now been improved by adding calcium chloride to the flask liquor after the removal of the readily steam-volatile 4-nitro-3-hydroxybenzaldehyde, and continuing the steam-distillation. The colourless needles of 2-nitro-3-hydroxybenzaldehyde so obtained had m. p. 157° (Friedländer and Schenck, *Ber.*, 1914, **47**, 3043, 3046, give m. p. 152°; Henry and Sharp, *loc. cit.*, give m. p. 157°). The p-*nitrophenylhydrazone* crystallised from aqueous 80% acetic acid in iridescent orange needles, m. p. 250° (decomp.) [Hodgson and Beard, *loc. cit.*, give m. p. 240—250° (decomp.)] (Found: N, 18·7. Calc. for $C_{13}H_{10}O_5N_4$: N, 18·5%).

Iodination of 2-Nitro-3-hydroxybenzaldehyde.—When a saturated aqueous solution of the aldehyde was vigorously shaken with excess of iodine, 4 : 6-di-iodo-2-nitro-3-hydroxybenzaldehyde separated as a crystalline precipitate. It was freed from admixed iodine, and recrystallised from aqueous 70% alcohol, forming colourless needles, m. p. 158° (Henry and Sharp, *loc. cit.*,

give m. p. 154·5°) (Found : I, 60·4. Calc. for $C_7H_4O_4NI_2$: I, 60·6%). The p-*nitrophenylhydrazone* crystallised from aqueous 70% alcohol in orange-yellow needles, m. p. 250° (decomp.) (Found : I, 45·6. $C_{13}H_8O_5N_4I_2$ requires I, 45·8%).

4-Nitro-3-hydroxybenzaldehyde could not be iodinated under similar conditions.

Iodination of 6-*Nitro-3-hydroxybenzaldehyde*.—A suspension of the aldehyde (6 g.) and iodine (9·2 g.) in chloroform (80 c.c.) was shaken vigorously for 3 hours with mercuric oxide (10 g.); the solid was then collected and extracted with aqueous 10% sodium carbonate. On acidification of the extract with dilute hydrochloric acid, 2 : 4-di-iodo-6-nitro-3-hydroxybenzaldehyde was precipitated; it crystallised from aqueous 50% alcohol in cream-coloured needles, m. p. 142° (Henry and Sharp, *loc. cit.*, give m. p. 142°). The p-*nitrophenylhydrazone* crystallised from glacial acetic acid in orange-yellow needles, m. p. 244° (decomp.) (Found : N, 10·3. $C_{13}H_8O_5N_4I_2$ requires N, 10·1%).

4-Nitro-3-hydroxybenzaldehyde remained unchanged when subjected to the above procedure.

2 : 4-*Di-iodo-6-nitro-3-methoxybenzaldehyde* was obtained when the hydroxy-aldehyde (1 g.), ground intimately with moist potassium carbonate (1 g.), was treated with methyl sulphate (3 c.c.), and the mixture heated on the water-bath for 3 hours, stirred into a large excess of saturated aqueous sodium carbonate, and again heated for 2 hours. The insoluble ether was crystallised once from alcohol and once from aqueous 80% acetic acid; it was then obtained in buff needles, m. p. 142°, depressed by admixture with the unmethylated product (m. p. 142°) (Found : I, 58·4. $C_8H_5O_4NI_2$ requires I, 58·6%). The p-*nitrophenylhydrazone* crystallised from glacial acetic acid in deep orange needles, m. p. 220° (decomp.) (Found : N, 10·0. $C_{14}H_{10}O_5N_4I_2$ requires N, 9·8%).

Iodination of 2 : 6-*Dinitro-3-hydroxybenzaldehyde*.—The aldehyde (1 g.), dissolved in aqueous 10% sodium carbonate (100 c.c.), was stirred with iodine (1·2 g.) during the addition of aqueous 20% sodium hydroxide until the iodine had completely dissolved. After 1 hour, the solution was acidified with hydrochloric acid; the precipitated 4-*iodo*-2 : 6-*dinitro-3-hydroxybenzaldehyde* crystallised from water in long buff needles, m. p. 168° (Found : I, 37·5. $C_7H_3O_6N_2I$ requires I, 37·6%). The p-*nitrophenylhydrazone* crystallised from cellusolve in bright red needles, decomp. 310° (Found : I, 26·6. $C_{13}H_8O_7N_5I$ requires I, 26·9%).

Iodination of 4 : 6-*Dinitro-3-hydroxybenzaldehyde*.—A solution of 4 : 6-dinitro-3-hydroxybenzaldehyde prepared by the method of Hodgson and Beard (J., 1927, 2378) was poured on ice and, after filtration, shaken with excess of iodine; the pure 2-*iodo*-4 : 6-*dinitro-3-hydroxybenzaldehyde* which separated was recrystallised from water, forming long, pale yellow needles, m. p. 106·5° (Found : N, 8·5; I, 37·4. $C_7H_3O_6N_2I$ requires N, 8·3; I, 37·6%). The p-*nitrophenylhydrazone* crystallised from glacial acetic acid in scarlet needles, m. p. 282° (decomp.) (Found : I, 26·8. $C_{13}H_8O_7N_5I$ requires I, 26·9%).

Action of Nitric Acid on 2 : 6-*Di-iodo-3-hydroxybenzaldehyde*.—The aldehyde, left in contact with dilute (30%) nitric acid, was gradually converted into 2 : 6-di-iodo-4-nitro-3-hydroxybenzaldehyde, which crystallised from water in yellow needles, m. p. 123° [Henry and Sharp, *loc. cit.*, give m. p. 122° (corr.)] (Found : I, 60·7. Calc. for $C_7H_3O_4NI_2$: I, 60·6%), formed a red *sodium* salt (Found : Na, 5·0. $C_7H_2O_4NI_2Na$ requires Na, 5·2%), and was oxidised by alkaline permanganate to give Henry and Sharp's di-iodo-4-nitro-3-hydroxybenzoic acid. The p-*nitrophenylhydrazone* crystallised from glacial acetic acid in brick-red needles, m. p. 218° (decomp.) (Found : N, 10·2. $C_{13}H_8O_5N_4I_2$ requires N, 10·1%).

Action of Nitric Acid on 4 : 6-*Di-iodo-2-nitro-3-hydroxybenzaldehyde*.—Although this aldehyde remained unaffected by nitric acid (*d* 1·42), it slowly dissolved in a stronger acid (*d* 1·5), and when the solution was poured on ice and saturated with sodium nitrate, 6-*iodo*-2 : 4-*dinitro-3-hydroxybenzaldehyde* separated in yellow needles, which were recrystallised from water; m. p. 160° (Found : I, 37·3. $C_7H_3O_6N_2I$ requires I, 37·6%).

The Action of Iodine on 4-*Nitro-3-hydroxybenzaldehyde*.—A solution of the aldehyde (1 g.) in saturated aqueous sodium carbonate was treated with iodine (1·5 g.) dissolved in aqueous potassium iodide (1·5 g.), and kept until the colour of the iodine had disappeared. On acidification with hydrochloric acid, 4-nitro-3-hydroxybenzoic acid separated; it crystallised from aqueous 50% alcohol in yellow needles, m. p. 238° [Henry and Sharp, *loc. cit.*, give m. p. 235° (corr.)] (Found : N, 7·8. Calc. for $C_7H_5O_5N$: N, 7·6%), and did not depress the m. p. of an authentic specimen prepared by the oxidation of 4-nitro-3-hydroxybenzaldehyde with alkaline permanganate.

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18. *The Identity of Dacrene and Sciadopitene with Phyllocladene.*

By Lindsay H. Briggs.

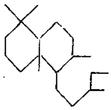
In 1910 Baker and Smith (" Pines of Australia," p. 419) described the isolation of the first crystalline diterpene, phyllocladene, from the leaf-oil of *Phyllocladus rhomboidalis* (Celery Top Pine). From its stability towards oxidising agents and bromine in acetic acid solution it appeared to be saturated, but without further evidence a formula was proposed on the assumption that it was derived from two molecules of pinene.

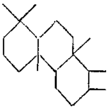
In the following pages a crystalline diterpene is described, which has been isolated from the leaf-oils of *Phyllocladus alpinus* and *Araucaria excelsa*. This substance is found to be identical with the diterpenes phyllocladene (*loc. cit.*), dacrene (Goudie, *J. Soc. Chem. Ind.*, 1923, **42**, 357T; Aitken, *ibid.*, 1928, **47**, 223T; Blackie, *ibid.*, 1929, **48**, 357T; 1930, **49**, 26T), sciadopitene (Nishida and Uoda, *Bull. Agric. Chem. Soc. Japan*, 1935, **11**, 95), and an unnamed diterpene from the leaf-oil of *Dacrydium cupressinum* (Dr. J. R. Hosking, private communication). The identity of these compounds has been established by mixed melting point determinations of the diterpenes themselves and also by a comparison of the physical constants of their derivatives. The names dacrene and sciadopitene should therefore be removed from the literature. These observations are of botanical interest, showing the wide occurrence of phyllocladene in different genera.

Phyllocladene is readily and completely isomerised by alcoholic sulphuric acid to *iso*phyllocladene (cf. Nishida and Uoda, *loc. cit.*). This ready isomerisation would indicate that the *iso*-hydrocarbon might be a natural product. No such compound, however, could be found described in the literature, but the physical constants of one of the four diterpenes isolated by Kawamura (*Bull. Imp. Forestry Exp. Sta. Tokyo*, 1931, No. 31, 93) from the leaf-oil of *Sciadopitis verticcilata* suggest that this is the optical antipode of *iso*-phyllocladene. Its m. p. is 111—112°, $[\alpha]_D^{11°}$ — 24·5° (chloroform), the monohydrochloride has m. p. 105—107° (decomp.) and the dihydro-derivative m. p. 71—72°: the corresponding constants of *iso*phyllocladene and derivatives are 110·5—112°, $[\alpha]_D^{17°}$ + 23·4° (chloroform), 105—107° (decomp.), 73—74°, respectively.

Hydrogenation of phyllocladene in the presence of palladised charcoal gives α-dihydrophyllocladene and from the mother-liquors a second isomer, β-dihydrophyllocladene, has been isolated in small yield. These are identical with the two dihydrophyllocladenes obtained by C. W. Brandt (private communication) by hydrogenation in the presence of platinum oxide. The two dihydro-compounds are probably stereoisomers.

Biogenetic relationships suggest that phyllocladene may be related to the oxygenated diterpene compounds of carbon skeleton (I), isolated from the wood of *Dacrydium colensoi* and *D. biforme* by Hosking and Brandt (*Ber.*, 1934, **67**, 1173; 1935, **68**, 37, 286, 1311; Hosking, *ibid.*, 1936, **69**, 780). Phyllocladene is tetracyclic and probably contains the phenanthrene structure (II), together with an additional 3- or 4-membered ring.

(I.) 

 (II.)

Experimental.

Phyllocladene.—The crude diterpenes from the essential oils of *Phyllocladus alpinus* and *Araucaria excelsa* (forthcoming publication) crystallised from ethyl and methyl alcohol in glistening plates, m. p. 96°, raised to 98° on recrystallisation; $[\alpha]_D^{23°}$ + 15·8° (chloroform). The m. p.'s of both hydrocarbons were not depressed by admixture, nor by admixture with an authentic specimen of phyllocladene kindly provided by Dr. F. Lions. No m. p. depression occurred by admixture with dacrene (private communication from the late Professor Inglis), sciadopitene (kindly forwarded by Prof. K. Nishida), and with the diterpene isolated from *D. cupressinum* (Hosking, *loc. cit.*) [Found: C, 88·1; H, 11·7; *M*, 268 (ebullioscopic in dioxan); M.R. 84·1 (from constants of a solution in cedrene). Calc. for $C_{20}H_{32}$: C, 88·2; H, 11·8%;

M, 272. $C_{20}H_{32}|_{\bar{1}}^{=}$ requires M.R. 85·29]. The diterpene gives a faint but definite yellow coloration with tetranitromethane. With concentrated sulphuric acid it gives a yellow coloration, which turns brown with a yellowish-green fluorescence on the addition of acetic anhydride.

*iso*Phyllocladene.—Phyllocladene (2 g.), partly suspended in 10% alcoholic sulphuric acid (6·5 c.c.), is completely converted into *iso*phyllocladene on heating at 100° for a few minutes. The product (theoretical yield), collected after pouring into water, crystallised from methyl or ethyl alcohol in needles, m. p. 108—109°, raised to 110·5—112° after further recrystallisations from acetic acid, $[\alpha]_D^{17^\circ}$ + 23·4° (chloroform), M.R. (calculated from constants of a solution in cedrene) 84·4; $C_{20}H_{32}|_{\bar{1}}^{=}$ requires M.R. 85·3. The m. p. was not depressed by a sample prepared from 30 mg. of authentic phyllocladene. The m. p.'s and rotations recorded for *iso*dacrene and *iso*sciadopitene are 107°, $[\alpha]_D$ + 48·4°, and 108—109°, $[\alpha]_D^{20^\circ}$ 22·13 (chloroform) respectively. The large rotation of *iso*dacrene is possibly due to a factorial error. It gives a yellow coloration with tetranitromethane, and the same coloration with sulphuric acid and acetic anhydride as that with phyllocladene.

Phyllocladene Hydrochloride.—This was prepared by passing dry hydrogen chloride into a solution of the hydrocarbon in absolute ether at − 15°; on concentration of the solvent it crystallised in plates, m. p. 105—107° (slight decomp.). Dacrene hydrochloride (Aitken, Blackie, *locc. cit.*) has m. p. 108·5°, and sciadopitene hydrochloride m. p. 106° (decomp.).

α- and β-Dihydrophyllocladene.—Phyllocladene (100 mg.) in glacial acetic acid solution (6 c.c.) was hydrogenated in the presence of palladised charcoal. After removal of the catalyst, water was added, and the crystalline product recrystallised from alcohol, forming thin plates, m. p. 74—74·5°. From the mother-liquors another isomer was isolated, m. p. 55°. Neither of these gave a depression on admixture with the isomers prepared by C. W. Brandt (see p. 79). Both compounds are dihydro-derivatives by analysis (Brandt) and give no coloration with tetranitromethane.

Phyllocladene Nitrosochloride.—To phyllocladene (2 g.), mostly suspended in glacial acetic acid (2 c.c.) and amyl nitrite (1·72 g.) at − 17°, was added drop by drop a mixture of concentrated hydrochloric acid (1·3 c.c.) and glacial acetic acid (2 c.c.), the whole being well shaken. The green viscous oil produced solidified overnight in the ice-chest. It was collected, washed with alcohol (yield, 1·32 g.), and dissolved in the minimum amount of chloroform, acetone added, and the whole left in a freezing mixture. The nitrosochloride crystallised in colourless plates, m. p. 128° (decomp.) (Found: N, 4·2, 4·3. Calc. for $C_{20}H_{32}ONCl$: N, 4·2%). Sciadopitene nitrosochloride (*loc. cit.*) has m. p. 127—128° (decomp.). It gives only a slight discoloration with concentrated sulphuric acid–acetic anhydride.

Phyllocladene Nitrosate.—To a suspension of phyllocladene (2 g.) in glacial acetic acid (2 c.c.) and amyl nitrite (1·72 c.c.) cooled to − 18°, was added drop by drop, with continual shaking, a mixture of concentrated nitric acid (1·6 c.c., *d* 1·43) and glacial acetic acid (2 c.c.). The solid formed overnight in the ice-chest from the pale green oil produced was filtered off and well washed with alcohol (yield, 1·46 g.). It crystallised in colourless prisms, m. p. 129·5° (decomp.), from a solution in the minimum amount of chloroform after addition of acetone in excess and leaving in the ice-chest. Sciadopitene nitrosate has m. p. 126—127° (decomp.) (Found: N, 7·65, 7·9. Calc. for $C_{20}H_{32}O_4N_2$: N, 7·7%).

The author is indebted to Dr. R. A. Robinson for determinations of molecular weight and molecular refractions, to the Royal Society of New Zealand for the loan of apparatus, and to the Chemical Society for a grant.

UNIVERSITY COLLEGE, AUCKLAND, NEW ZEALAND. [*Received, November 19th*, 1936.]

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19. *The Chemistry of* Aspergillus *Colouring Matters. Part I.*

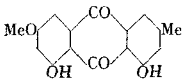
By H. RAISTRICK, ROBERT ROBINSON, and A. R. TODD.

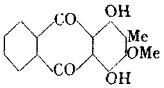
GOULD and RAISTRICK (*Biochem. J.*, 1934, **28**, 1640) have described yellow, orange and red crystalline pigments occurring in the mycelia of various species of *Aspergillus* of the *A. glaucus* series when grown on a modified Czapek–Dox medium with glucose as the source of carbon.

The yellow and orange colouring matters are related, and have been termed flavoglaucin ($C_{19}H_{28}O_3$) and auroglaucin ($C_{19}H_{22}O_3$) respectively; on the other hand rubroglaucin,

$C_{16}H_{12}O_5$, has the character of a polyhydroxyanthraquinone and does not in the least resemble the other pigments.

In working up crude flavoglaucin from *A. glaucus* Link, we have been able to isolate a small quantity of a fourth colouring matter, which proved to be identical with the emodin monomethyl ether isolated from *Ventilago madraspatana* Gärtn. by A. G. Perkin and Hummel (J., 1894, **65**, 943) and later found widely distributed in nature. This substance, often called physcion, was obtained by Jowett and Potter (J., 1903, **83**, 1330) by the methylation of emodin with methyl iodide and methyl-alcoholic sodium methoxide. According to Eder and Hauser (*Helv. Chim. Acta*, 1925, **8**, 140) physcion is 4 : 5-dihydroxy-7-methoxy-2-methylanthraquinone (I) and this suggestion is very probably correct in

(I.) 

 (II.)

view of the synthesis of *Frangula* emodin itself (Eder and Widmer, *Helv. Chim. Acta*, 1923, **6**, 966; Adams and Jacobson, *J. Amer. Chem. Soc.*, 1924, **46**, 1316) and the methylation mentioned above.

A specimen obtained by Perkin and Hummel had been preserved in the collection of the Department of Colour Chemistry and Dyeing at Leeds University, and we are grateful to Professors A. G. Perkin and F. M. Rowe for the opportunity to make a direct comparison with our material.

Physcion has been known for many years as one of the so-called lichen acids occurring particularly in different species of *Xanthoria* and of *Placodium*. The isolation of physcion from species of *Aspergillus* is the first recorded instance of any mould metabolic product which is identical with one of the lichen acids, although several very closely related substances have been isolated. This observation is of importance, since it indicates that it is the fungal and not the algal half of the lichen symbiont which synthesises the lichen acids.

Rubroglaucin.—The melting point of rubroglaucin is now found to be 180—181° (Gould and Raistrick, *loc. cit.*, gave m. p. 172—173°), but the identity of the substance is not in doubt because most of the material examined was derived from *A. ruber* following the earlier procedure. It has also been isolated in small relative quantity from *A. albidus* and *A. glaucus mut. alba*. This substance, $C_{16}H_{12}O_5$, contains a methoxyl group and has the composition and properties of a dihydroxymethoxymethylanthraquinone. Actually it affords a diacetyl derivative and gives 2-methylanthracene on distillation with zinc dust.

Some further light on its constitution is thrown by the absence of adjective dyeing properties (no vicinal hydroxyls) and by its insolubility in aqueous sodium carbonate (no β-hydroxyl groups). On demethylation, however, a mordant dye is obtained and this is soluble in alkali carbonates. Furthermore, the solutions of rubroglaucin in acetic acid and some other solvents are yellow with a green fluorescence; this indicates the quinizarin group (compare the present authors, *Biochem. J.*, 1934, **28**, 567). It would appear that rubroglaucin should be a methoxy-1 : 4-dihydroxy-β-methylanthraquinone and we thought (II) the most likely of the various isomerides because the solution of rubroglaucin in sulphuric acid is bluer in tone than that of purpurin in this solvent. The inclusion of the methyl group in the hydroxylated ring of purpurin seemed to be the only plausible way of providing an explanation of this contrast, always assuming that demethylated rubroglaucin is a homologue of purpurin.

Accordingly, 1 : 3 : *4-trihydroxy-2-methylanthraquinone* was synthesised and this substance proved to be very similar to purpurin in its properties and quite different from demethylated rubroglaucin.

Hence it is very probable that demethylated rubroglaucin, despite its mordant dyeing properties, is not a methylpurpurin and, as it must be a quinizarin, it cannot be an alizarin derivative. Its solubility in aqueous alkali carbonates shows that it is not a 1 : 4 : 5-trihydroxyanthraquinone and consequently it must be a 1 : 4 : 6-trihydroxy-β-methyl-

anthraquinone. Rubroglaucin must be a 6-methoxy-1 : 4-dihydroxy-β-methylanthraquinone and the methyl group may be in one of the positions 2, 3, and 7. A decision will be sought by synthesis. Demethylated rubroglaucin could not be freed from a molecule of water, even by sublimation, and the analytical figures tallied with the formula $C_{15}H_{12}O_6$ ($C_{15}H_{10}O_5,H_2O$). A very small amount was available and the triacetate could not be recrystallised to constant melting point; its analysis, however, was satisfactory, agreeing with the formula $C_{21}H_{16}O_8$ or $C_{15}H_7O_2(OAc)_3$. Our synthetic 2-methylpurpurin was also found to retain $1H_2O$ very tenaciously, and there is no reason to doubt the view that demethylated rubroglaucin is a trihydroxymethylanthraquinone.

Flavoglaucin and Auroglaucin.—The compositions attributed to the yellow and the orange pigment of Gould and Raistrick (*loc. cit.*) have been confirmed by fresh analyses and by the preparation of derivatives. Flavoglaucin is $C_{19}H_{28}O_3$ and auroglaucin is $C_{19}H_{22}O_3$. The difference is accounted for by the fact that auroglaucin contains three double bonds more than flavoglaucin. Partial hydrogenation ($3H_2$ to flavoglaucin and $6H_2$ to auroglaucin) gave one and the same colourless solid, m. p. 111°, which was not quite homogeneous but was composed mainly of an unsaturated alcohol, $C_{19}H_{32}O_2$, yielding a characteristic, homogeneous, *phenylurethane*.

On microhydrogenation in presence of platinum, auroglaucin and flavoglaucin took up volumes of hydrogen corresponding with 10 and 7 molecular proportions respectively. On a larger scale flavoglaucin absorbed rather more than $7H_2$ and afforded a colourless liquid giving analytical figures agreeing with $C_{38}H_{76}O$, and probably consisting of a mixture of $C_{19}H_{38}O$ with $C_{19}H_{38}$. The relevant equation is $C_{19}H_{28}O_3 + 7H_2 = C_{19}H_{38}O + 2H_2O$, and reduction to $C_{19}H_{38}$ would account for the hydrogen absorbed in excess of the theoretical volume. Oxidation of flavoglaucin by means of potassium permanganate in pyridine or acetone solution afforded oxalic acid, *n*-octoic acid, probably acetic acid, and unidentified acids giving high-boiling methyl esters.

Attempts to determine the functions of the oxygen atoms showed that the substances are ketonic (dinitrophenylhydrazones) and the Zerewitinoff determinations indicated the presence of two hydroxyl groups in flavoglaucin and auroglaucin. In addition a crystalline *phenylurethane* was obtained from auroglaucin. The third oxygen may be present as a protected hydroxyl group or as a readily ruptured ether linkage. In the latter case the Zerewitinoff results must be interpreted as due to enolisation of the ketone. Auroglaucin condenses with *o*-phenylenediamine with elimination of only $1H_2O$, but the product cannot be diazotised; hence it would appear that auroglaucin may be an αβ-unsaturated ketone.

These data do not allow us to advance a constitutional formula, but it may be pointed out that full hydrogenation provides some evidence of the existence of one carbocyclic structure and it is not excluded that this may be a benzene ring. On the other hand, no degradation product supporting this hypothesis has been isolated.

The formation of *n*-octoic acid by permanganate oxidation of flavoglaucin shows that the group $CH_3{\cdot}[CH_2]_6{\cdot}C⫶$ is contained in the molecule and the full structure might be that of a benzene derivative containing a long aliphatic chain or chains, two hydroxyl groups, a carbonyl group, and a double bond. One of the hydroxyl groups might be replaced by a readily ruptured cyclic ether linkage. On the benzenoid hypothesis the double bond would then need to be saturated. If the colouring matters do not contain a benzene nucleus, the number of possible isomerides is greatly increased, and it is difficult to devise a plausible formula. The investigation is being continued.

The flavoglaucin used in this research was obtained from *A. amstelodami*, *A. glaucus* Link, *A. novus*, *A. mongolicus*, *A. albidus*, *A. glaucus mut. alba* and *A. oriolus*. The auroglaucin was derived from *A. novus*, *A. Scheelei*, *A. Dierckxii*, *A. fumigatoides*, *A. mollis*, *A. profusus*, *A. argillaceus*, *A. disjunctus*, *A. pseudoglaucus*, and *A. oriolus*.

EXPERIMENTAL.

Flavoglaucin.—The crude pigment from the various species is difficult to purify on account of its ready solubility in many solvents and gummy impurities hinder the crystallisations. The following method was adopted in order to obtain pure flavoglaucin. The crude material

was extracted (Soxhlet) with light petroleum (b. p. 40—60°); flavoglaucin separated from the extract on cooling. This recrystallisation by extraction was repeated, and the product further purified by repeated crystallisation from 75% alcohol. It was obtained as pale yellow platelets, m. p. 100°, sufficiently pure for most purposes. Final purification by crystallisation from hexane gave a product, m. p. 103° [Found: C, 74·9, 75·0; H, 9·0, 8·9; *M* (Rast), 299, 306. Calc. for $C_{19}H_{28}O_3$: C, 75·0; H, 9·3%; *M*, 304].

Flavoglaucin contains no methoxyl groups, and estimation of hydroxyl groups (Zerewitinoff) gave OH, 10·9, 11·3% in pyridine solution (Calc. for 2OH, 11·2%). Estimation of side-chain methyl groups (Kuhn and Roth) indicated the presence of one such group (CrO_3 oxidation gave 0·9, 0·9 mol. of acetic acid).

Flavoglaucin is insoluble in water but readily soluble in organic solvents with the exception of light petroleum, in which it is but sparingly soluble in the cold. Its solutions are intensely yellow. The following reactions were noted: (1) In alcoholic solution it gives a dull green colour with ferric chloride which quickly fades and becomes dirty brown. (2) It is not immediately soluble in aqueous sodium hydroxide but dissolves slowly to a solution which, at first orange, fades to yellowish-brown, becomes turbid and froths on shaking. A similar effect is produced after prolonged standing with sodium carbonate solution. (3) The brownish solution in concentrated sulphuric acid darkens rapidly on heating. (4) A fine ruby-red coloration is produced on the addition of a saturated solution of antimony trichloride in chloroform. (5) A solution in glacial acetic acid is very slowly decolourised by hydrogen peroxide. (6) Potassium permanganate is instantly decolourised in acetone solution, as also is bromine in chloroform solution. (7) In alcoholic solution it is readily reduced by zinc dust and a little concentrated hydrochloric acid with formation of a colourless crystalline substance soluble in alcohol or ether to a colourless solution with a violet fluorescence. This product is gradually oxidised in the air (or by means of ferric chloride) to a brownish substance which is not identical with the original material. (8) Micro-zinc-dust-distillation gave traces of a brown oil with a pungent odour which did not crystallise or form a picrate.

Flavoglaucin and o-*Phenylenediamine.*—A solution of flavoglaucin (37 mg.) and *o*-phenylenediamine (16 mg.) in alcohol (5 c.c.) was refluxed for 45 minutes; on dilution with a little water a yellow crystalline solid separated. Recrystallised from alcohol, it formed pale yellow needles, m. p. 161° (Found in material dried in a vacuum over phosphoric oxide: C, 75·8; H, 8·4; N, 7·3. $C_{25}H_{34}O_2N_2$ requires C, 76·1; H, 8·6; N, 7·1%). The *substance*, although appearing to react with nitrous acid in some way, did not undergo diazotisation. An attempt to obtain a crystalline acetyl derivative from it by acetylation afforded a gummy product.

Flavoglaucin 2 : 4-*Dinitrophenylhydrazone.*—Flavoglaucin (50 mg.), dissolved in a little warm methyl alcohol, was added to a solution of 2 : 4-dinitrophenylhydrazine (70 mg.) in methyl alcohol containing a little hydrogen chloride. The solution immediately became orange-red and after heating on the steam-bath for 15 minutes it was cooled. The crystalline product which separated was recrystallised from chloroform–alcohol. It formed small, deep red needles, m. p. 179—181°, which on drying over phosphoric oxide in a vacuum became opaque, possibly by loss of solvent of crystallisation. This *substance* seems to exist in two modifications, as it crystallised initially from the reaction mixture as orange needles, m. p. 186—187° (Found: C, 61·8; H, 6·1; N, 12·2. $C_{25}H_{32}O_6N_4$ requires C, 62·0; H, 6·1; N, 11·6%).

Other Derivatives of Flavoglaucin.—Acetylation with acetic anhydride gave an oil, as also did treatment with phenyl *iso*cyanate. Flavoglaucin forms a colourless or only very faintly coloured oxime, but it is difficult to crystallise. The phenylhydrazone was obtained as a yellowish crystalline solid which was rather unstable and tended to decompose partly during purification.

Flavoglaucin (40 mg.) was heated on the steam-bath during 30 minutes with a solution of excess of phenylhydrazine in 90% acetic acid. On addition of a little water and cooling, the *product* separated as yellowish crystals. It separated from dilute acetic acid as small yellowish prisms, m. p. 137° (Found: N, 7·4. $C_{25}H_{34}O_2N_2$ requires N, 7·1%).

Auroglaucin.—The crude auroglaucin is readily purified by recrystallisation from alcohol, forming fine orange-red needles, m. p. 153° [Found: C, 76·5, 76·7; H, 7·2, 7·3; *M* (Rast), 297, 298. Calc. for $C_{19}H_{22}O_3$: C, 76·5; H, 7·5%; *M*, 298].

Auroglaucin contains no methoxyl groups and estimation of hydroxyl groups (Zerewitinoff) gave a value between one and two hydroxyls (Found: OH, 8·9, 9·5 at 24°; 9·5, 9·8 at 95° in anisole. $C_{19}H_{22}O_3$ requires 1OH, 5·7; 2OH, 11·4). Estimation of side-methyl groups by chromic acid oxidation (Kuhn–Roth) gave 1·3 mols. of acetic acid, corresponding probably to one side-methyl group and some volatile acid from the end of the chain (see p. 82).

Auroglaucin is insoluble in water and rather sparingly soluble in most organic solvents, but it dissolves readily in chloroform. Its solutions are intensely yellow at moderate concentrations—much more intense than corresponding solutions of flavoglaucin. The following properties were noted : (1) With ferric chloride in alcoholic solution it gives a red colour, fading to brown. (2) It is not immediately soluble in aqueous sodium hydroxide but, like flavoglaucin, dissolves slowly. The solution is at first cherry-red, but becomes dirty brown and turbid. (3) With concentrated sulphuric acid a reddish purple coloration is produced; on warming, charring occurs. (4) Antimony trichloride in chloroform gives a brownish-red colour, fading rapidly to greenish-brown and becoming olive-green on standing. (5) Glacial acetic acid solutions are very slowly decolourised by hydrogen peroxide. (6) Auroglaucin in acetone decolourises potassium permanganate instantaneously; bromine is decolourised by auroglaucin in chloroform solution. (7) The behaviour on reduction with zinc and hydrochloric acid and on zinc-dust distillation was the same as that of flavoglaucin.

Auroglaucin and o-*Phenylenediamine.*—A solution of auroglaucin (100 mg.) and *o*-phenylenediamine (50 mg.) in alcohol (*ca.* 10 c.c.) was refluxed for 45 minutes. On cooling, small yellow crystals separated, which were collected and recrystallised from alcohol. The *product* formed small yellow rods, m. p. 185° (decomp.); on exposure to the air they gradually become brown (Found : C, 74·0; H, 7·1; N, 7·2; loss at 100° in a high vacuum over phosphoric oxide, 4·2. $C_{25}H_{28}O_2N_2,H_2O$ requires C, 73·9; H, 7·4; N, 6·9; H_2O, 4·4%).

A solution of the substance in acetic acid developed a red colour on the addition of concentrated hydrochloric acid; addition of sodium nitrite to this solution caused some change, a brownish substance being formed, but the product did not couple with β-naphthol in alkaline solution.

Auroglaucin 2 : 4-Dinitrophenylhydrazone.—A solution of auroglaucin (40 mg.) in warm methyl alcohol was added to a similar solution of 2 : 4-dinitrophenylhydrazine (56 mg.) in methyl alcohol containing a little hydrogen chloride. An orange-red precipitate was almost immediately formed. The mixture was heated on the steam-bath for 1 hour to ensure complete reaction and some decomposition occurred, the liquid becoming greenish-brown. On cooling, the *product* separated as small brick-red needles, which were recrystallised from chloroform–alcohol; m. p. 223—224° (Found : C, 62·6; H, 5·4; N, 12·0. $C_{25}H_{26}O_6N_4$ requires C, 62·7; H, 5·4; N, 11·8%).

Auroglaucin Phenylurethane.—A solution of auroglaucin (0·1 g.) and phenyl *iso*cyanate (0·5 g.) in dry benzene (*ca.* 8 c.c.) was heated under reflux for 4 hours. After distillation of half the solvent, the solution was cooled; the *phenylurethane* then separated. Recrystallised from alcohol, it formed pale yellow, slender rods, m. p. 161° (Found : C, 74·7; H, 6·4; N, 3·6. $C_{26}H_{27}O_4N$ requires C, 74·8; H, 6·5; N, 3·4%).

Acetylation of Auroglaucin.—When auroglaucin (0·1 g.) was boiled for 5 minutes with acetic anhydride (6 c.c.) and anhydrous potassium acetate (0·1 g.), a pale yellow solution was formed. The crystalline precipitate obtained on pouring into water was collected, washed with a little water, and recrystallised from alcohol as rapidly as possible. The product formed sheaves of yellowish needles, m. p. 108—109°. On keeping in a corked tube the crystals rapidly became opaque and slowly developed an orange colour. Analysis of the compound gave values quite unlike those for any simple acetate of auroglaucin [Found : C, 60·6, 60·5; H, 5·7, 5·5; CH_3·CO (by CrO_3 oxidation), 32·3, 32·3. Allowing for the 1·3 mols. of acetic acid produced from auroglaucin under the same conditions, we get CH_3·CO, 10·2%].

Catalytic Hydrogenation of Flavoglaucin and Auroglaucin.—In order to obtain good results in the hydrogenation of both pigments, it seems necessary to use considerable quantities of catalyst. Using ordinary platinum-black, it is possible to stop the hydrogenation at an intermediate stage as is described below. For complete hydrogenation a platinum–silica catalyst (Membranfilter A.G. No. 17) or highly active platinum-black should be used.

(A) *Partial hydrogenation.* (1) *Flavoglaucin.* A solution of flavoglaucin (0·257 g.) in glacial acetic acid (*ca.* 30 c.c.) was shaken with hydrogen in presence of platinum-black (0·5 g.). Absorption of hydrogen was at first very rapid, the equivalent of 2 mols. being taken up in 10 minutes, the third mol. requiring almost ½ hour more. The hydrogenation was stopped at this stage, the solution being only very faintly coloured (observed absorption, 63 c.c. Calc. for $3H_2$, 60 c.c.). The filtered solution was evaporated in a vacuum, and the pale yellowish residue was recrystallised several times from ether–light petroleum (b. p. 40—60°). The reduction *product* formed colourless needles (0·19 g.), m. p. 111° [Found : C, 76·9, 76·8; H, 10·8, 10·8; *M* (Rast), 260, 269. $C_{19}H_{32}O_2$ requires C, 78·1; H, 11·0%; *M*, 292].

The neutral substance is strongly unsaturated to potassium permanganate and non-ketonic.

It gives no coloration with ferric chloride in alcoholic solution. It yields on acetylation a colourless oil, but gives a crystalline bisphenylurethane with phenyl *iso*cyanate and hence contains two hydroxyl groups.

The substance (70 mg.) was dissolved in dry benzene (5 c.c.) and after addition of phenyl *iso*cyanate (0·3 g.) the solution was refluxed for 4 hours, and half the solvent then removed by distillation. On cooling and keeping overnight, the *phenylurethane* separated as colourless crystals. After recrystallisation from alcohol it formed globular aggregates of colourless needles, m. p. 160—161° after slight sintering at 157° (Found: C, 74·7; H, 7·9; N, 5·6. $C_{33}H_{42}O_4N_2$ requires C, 74·7; H, 7·8; N, 5·3%).

(2) *Auroglaucin.* A suspension of auroglaucin (0·254 g.) in glacial acetic acid (*ca.* 30 c.c.) was shaken with hydrogen in presence of platinum-black (0·5 g.). Hydrogen was at first rapidly absorbed, a volume corresponding to 4 mols. being taken up in some 15 minutes, the suspended material passing meanwhile into solution. During the next hour a further 2 mols. were absorbed; the hydrogenation was then stopped (absorption, 123 c.c. Calc. for $6H_2$, 120 c.c.). On evaporation of the filtered solution in a vacuum a pale yellow crystalline solid was obtained, which after several recrystallisations from ether–light petroleum (b. p. 40—60°) formed colourless needles (0·2 g.), m. p. 111° (Found: C, 76·9, 76·6; H, 11·0, 10·9%). This product was identical in all its properties with the partial reduction product of flavoglaucin already described and a mixture of the two substances showed no depression of melting point. The identity was confirmed by the preparation of the bisphenylurethane in the manner already described. The colourless needles after recrystallisation from alcohol had m. p. 160—161° after slight sintering at 157° and had all the properties of the phenylurethane obtained from the product of partial reduction of flavoglaucin; a mixed melting point with the latter showed no depression (Found: C, 74·4; H, 8·0; N, 6·0%).

From the composition of the bisphenylurethane it appears that the reduction product consists mainly of a substance $C_{19}H_{32}O_2$. The analysis figures quoted for the reduction product are obtainable with all samples irrespective of the mode of purification and it seems probable that the material obtained represents mixed crystals of $C_{19}H_{32}O_2$ with a small amount of another product containing 3 oxygen atoms. The possibility that the substance might contain less than 19 carbon atoms was entertained, but it is discounted by the result of reducing molten flavoglaucin in a stream of hydrogen in presence of platinum-black; the only volatile product which could then be detected was water.

(B) *Complete hydrogenation.* (1) Micro-hydrogenation (Dr. A. Winterstein, Heidelberg), with a platinum–silica catalyst containing 17% of platinum (differential method), gave the following results: Auroglaucin, $C_{19}H_{22}O_3$, absorbed 10 mols. of hydrogen; flavoglaucin, $C_{19}H_{28}O_3$, absorbed 7 mols. of hydrogen.

(2) *Hydrogenation of flavoglaucin.* Flavoglaucin (1 g.), dissolved in glacial acetic acid (60 c.c.), was shaken with hydrogen in presence of highly active platinum-black (2 g.). Absorption was at first rapid, but slowed down to a steady rate after some 3 mols. of hydrogen had been taken up. At this stage the solution became colourless and a quantity of colourless crystalline material separated, which dissolved again as the reduction proceeded. After 6 hours, absorption had practically ceased (observed absorption, 580 c.c. Calc. for $7H_2$, 550 c.c.). The filtered solution was evaporated in a vacuum on the steam-bath and the colourless viscous residue was fractionated in a vacuum; after two distillations it had b. p. *ca.* 173—175°/12 mm. (Found: C, 83·8; H, 13·7%). The analytical values suggested that this liquid was a mixture of an alcohol containing one oxygen atom with a hydrocarbon. Accordingly it was again shaken with hydrogen in acetic acid solution in presence of platinum-black, but very little hydrogen was absorbed; on working up as before and subjecting the product to two fractionations, we obtained a colourless liquid, b. p. *ca.* 173—175°/12 mm. (Found: C, 83·6; H, 13·8%). The product is apparently quite saturated, as it does not decolourise potassium permanganate or bromine water.

Oxidation of Flavoglaucin with Potassium Permanganate.—A preliminary experiment with flavoglaucin (1 g.) in acetone solution showed that oxidation with potassium permanganate produced mainly a mixture of liquid acids, from which an amide, m. p. 102—103°, was ultimately obtained. The oxidation was accordingly carried out with a larger quantity of material.

Flavoglaucin (5 g.) was dissolved in pyridine (200 c.c.) and treated with 4% aqueous potassium permanganate in portions of 46·25 c.c. (equiv. to 1 atom of oxygen) at room temperature, the mixture being shaken after each addition until the colour disappeared. After 12 portions had been added decolourisation of the added permanganate was less rapid and it became exceedingly slow when a total of 15 portions had been added. After keeping over-night, the

solution was decolourised by means of sulphur dioxide, filtered from some crystalline inorganic material, made slightly alkaline with potassium hydroxide, and concentrated to about half its bulk in a vacuum on the steam-bath. After being made strongly acid, the solution was extracted continuously with ether during about 24 hours. The ethereal extract was thrice shaken with small quantities of concentrated potassium hydroxide solution and then with a little water, the aqueous layer being added to the alkali extracts. After drying over anhydrous sodium sulphate, the ether was removed and a trace of a colourless oil, which had a strong odour resembling that of rue, was obtained. It did not possess ketonic properties, however, and did not crystallise. On account of the small amount produced, it was not further investigated.

The alkaline solution was acidified with concentrated hydrochloric acid and extracted seven times with ether and the combined ethereal extracts were dried over anhydrous sodium sulphate. After removal of most of the ether on the steam-bath, the residue, which had a rancid odour, was treated with excess of diazomethane in ethereal solution. The ether was removed from the solution of esters produced, by cautious distillation on the water-bath through a fractionating column. After removal of the ether the residue was distilled first at the ordinary pressure. A trace of ester, possibly methyl acetate, distilled with the last traces of ether at about 55°, but nothing further came over till the bath temperature rose to about 180°; the distillation was then continued under diminished pressure, affording: (1) b. p. 90—100°/14 mm. Colourless liquid with slight fruity odour (0·5 g.) (Found: C, 62·7; H, 9·7%); (2) b. p. 100—108°/14 mm., similar colourless liquid (0·5 g.) (Found: C, 61·4; H, 10·3%); (3) b. p. 150—180°/14 mm. Brownish thick liquid (0·45 g.), whose distillation was accompanied by some decomposition. The residue in the flask charred on further attempted distillation.

From the analytical results it seemed probable that fractions (1) and (2) were fatty ester mixtures of rather similar composition; fraction (3) was deemed too impure to render analysis of any value. The various fractions were converted into amides

On standing for 4 weeks with concentrated aqueous ammonia (5 c.c., *d* 0·880) in a stoppered flask, the fraction (1) dissolved gradually and the liquid became filled with colourless plates mixed with a white powdery material. The solid material was collected, dried, extracted with a little hot benzene and filtered (the residue—a white powder—did not melt below 320° but underwent gradual sublimation above 300°; it appeared from its properties to be oxamide). To the hot benzene solution an equal volume of light petroleum (b. p. 60—80°) was added, and the solution allowed to cool; colourless platelets then separated. After several such recrystallisations the amide was obtained as glistening rectangular platelets, m. p. 103—104°, identical in properties with the product from fraction (2) (see below), with which a mixed m. p. gave no depression.

The liquid fraction (2) was kept for 4 weeks with concentrated aqueous ammonia (5 c.c., *d* 0·880); it behaved exactly as fraction (1) and was worked up in the same way. A small quantity of oxamide was obtained, less than from (1), but the main product was the amide, m. p. 103—104° (Found: C, 66·7; H, 11·8; N, 9·8. Calc. for $C_8H_{17}ON$: C, 67·1; H, 11·9; N, 9·8%). *n*-Octoamide has m. p. 105° and comparison with a specimen of this substance prepared from synthetic *n*-octoic acid showed the above amide to be identical with it. A mixture of the two substances melted at 104—105°.

Isolation of Emodin Monomethyl Ether (Physcion) from the Metabolic Products of A. glaucus *Link.*—It was observed in working up the crude flavoglaucin (4·5 g.) from *A. glaucus* Link by light petroleum extraction that the extract had a pale reddish colour. On cooling and standing overnight, the flavoglaucin crystallised as usual, but in addition a small quantity of reddish crystalline material was observed to be present. The mixed solids were collected and digested with warm 75% alcohol; the flavoglaucin readily dissolved, leaving the red substance as a practically insoluble residue. This, recrystallised several times from chloroform–alcohol, formed brownish-orange needles (8 mg.), m. p. 203—204° (Found: C, 67·8; H, 4·8; MeO, 11·3. Calc. for $C_{16}H_{12}O_5$: C, 67·6; H, 4·2; 1MeO, 10·9%). The substance dissolved in concentrated sulphuric acid to a reddish-purple solution, was insoluble in cold dilute sodium carbonate solution but soluble in caustic alkalis with a ruby-red colour, and was a very feeble mordant dye. These properties correspond to those of emodin monomethyl ether, which has m. p. 203—204°, and comparison with an authentic specimen of this substance (from *Ventilago madraspatana*) established the identity of the material isolated from *A. glaucus* Link. A mixed melting point of the two samples showed no depression.

Rubroglaucin.—The material used was derived from *A. ruber* (Gould and Raistrick, *loc. cit.*). Purification can be effected by recrystallisation from butyl alcohol (or from alcohol, but the crystals then appear to be solvated), the colouring matter forming small red needles, m. p.

180—181° [Found: C, 67·2; H, 4·3; MeO, 10·7; *M* (Rast), 336. Calc. for $C_{16}H_{12}O_6$: C, 67·6; H, 4·2; MeO, 10·9%; *M*, 284]. The total amount of purified material available was some 300 mg.

Rubroglaucin is practically insoluble in water and is only sparingly soluble in organic solvents apart from chloroform, which dissolves it readily. It has all the properties of a hydroxyanthraquinone derivative. Insoluble in cold aqueous sodium carbonate, it dissolves readily in sodium hydroxide to a red-violet solution. Its solution in concentrated sulphuric acid is violet with a blue tinge, and its solution in acetic acid is yellow with a green fluorescence. Rubroglaucin possesses practically no dyeing properties when applied to mordanted cotton.

Rubroglaucin from A. albidus.—The orange-coloured extract of crude flavoglaucin from *A. albidus* in light petroleum (b. p. 40—60°) showed a green fluorescence. On cooling and keeping, the flavoglaucin which separated was contaminated with a red crystalline substance present in small quantity. When the solid material was digested with warm 80% alcohol, the flavoglaucin dissolved, leaving the red substance. The latter, after several recrystallisations from alcohol, formed small red needles, m. p. 180—181°, identical in all properties with rubroglaucin; a mixed m. p. with the latter showed no depression (Found: C, 66·5, 66·5; H, 4·3, 4·3. Calc. for $C_{16}H_{12}O_6$,$0·5C_2H_5·OH$: C, 66·4; H, 4·9%). The quantity obtained in this way was approximately 30 mg.

The crude flavoglaucin from *A. glaucus mut. alba* gave on similar treatment some 6 mg. of rubroglaucin.

Rubroglaucin Acetate.—Rubroglaucin (20 mg.) was heated for a few minutes with acetic anhydride containing a trace of sulphuric acid. The yellow solution was poured into water, and the *acetate* collected and recrystallised twice from dilute acetic acid. The yellow needles, m. p. 226—228°, appeared to contain water of crystallisation (Found: C, 62·6; H, 4·4; MeO, 7·9. $C_{20}H_{16}O_7$,H_2O requires C, 62·2; H, 4·7; MeO, 8·0%).

2-Methylanthracene from Rubroglaucin.—Rubroglaucin (90 mg.) was subjected to zinc dust distillation in six portions of 15 mg. each, and the combined distillates, which took the form of a faintly yellowish, crystalline solid with a greenish fluorescence, were recrystallised several times from alcohol, affording colourless leaflets with a weak greenish fluorescence, m. p. 198°. A mixture of the substance with 2-methylanthracene (m. p. 204°) melted at 202°, but a mixture with anthracene (m. p. 212°) melted at 182—188°. There can be little doubt but that this product is 2-methylanthracene.

Demethylation of Rubroglaucin.—Rubroglaucin (100 mg.) was heated with concentrated sulphuric acid (2 c.c.) at 140—150° during 20 minutes. The solution was cooled, diluted with water, and the mixture boiled to coagulate the brownish precipitate, which was then collected, washed with water, dried, and recrystallised from chloroform–alcohol. Some decomposition had evidently occurred during the heating with sulphuric acid, as a large proportion of the crude product was dark in colour and did not dissolve in chloroform. The recrystallised product formed red needles, m. p. 217—218°, and two further crystallisations, followed by sublimation in a vacuum at 180°, were carried out before analysis. The bright red needles had m. p. 220° (Found: C, 62·7, 62·7; H, 4·2, 4·1. $C_{15}H_{10}O_5$,H_2O requires C, 62·5; H, 4·2%). The *triacetate* crystallised from acetic acid in yellow needles (Found in material dried at 150° in a high vacuum: C, 63·4; H, 4·1. $C_{21}H_{16}O_8$ requires C, 63·6; H, 4·0%).

The demethylated product, presumably a methyltrihydroxyanthraquinone, retaining $1H_2O$, resembles rubroglaucin in its colour reactions, but, unlike the latter, it is readily soluble in cold aqueous sodium carbonate solution. It is, moreover, a good mordant dye.

Synthesis of 1 : 3 : *4-Trihydroxy-2-methylanthraquinone.*—*2-Hydroxy-4-methoxy-3-methylacetophenone.* Resacetophenone (20 g., 1 mol.) was dissolved in a solution of potassium hydroxide (25 g., 6 mols.) in methyl alcohol (250 c.c.) contained in a flask fitted with a reflux condenser. Methyl iodide (62·5 g., 6 mols.) was then added in three portions, the flask being immersed in water at about 15°. When all had been added, the mixture was gently refluxed until the alkaline reaction of the liquid disappeared (4—5 hours; a little more methyl iodide may be added towards the end if necessary). After removal of the methyl alcohol, water was added to the residue, and the mixture extracted with ether. The ethereal extract was shaken once with excess of potassium hydroxide solution, dried, and evaporated. The residual reddish oil solidified almost at once, and on recrystallisation from light petroleum (b. p. 80—100°) furnished 2-hydroxy-4-methoxy-3-methylacetophenone as almost colourless platelets, m. p. 83—84° (yield, 5—6 g.); the alkaline extract on acidification and steam-distillation gave paeonol (*ca.* 3 g.).

2 : 3 : 6-Trimethoxytoluene. 2-Hydroxy-4-methoxy-3-methylacetophenone (10·8 g.) was

suspended in a mixture of *N*-sodium hydroxide (60 c.c.) and methyl alcohol (30 c.c.), and 3% hydrogen peroxide (51 c.c.) added under coal gas. After a short time the mixture became warm and much of the suspended material passed into solution, the liquid meanwhile acquiring a brownish tint. When the reaction had subsided and the flask cooled to room temperature, water (*ca.* 25 c.c.) was added, and unchanged initial material (3 g.) separated. The filtrate was acidified and extracted several times with ether, the extracts dried, and the ether removed, leaving a dark oily residue. This was dissolved in xylene (100 c.c.) and, after addition of anhydrous potassium carbonate (20 g.) and methyl sulphate (15 g.), the mixture was refluxed for 6 hours and then distilled in steam. The xylene came over first, followed by the desired methyl ether. The xylene layer was separated, dried, and the solvent removed cautiously by distillation through a short column. The residue, a colourless odourless liquid, had b. p. 145—147°/14 mm. (yield, 4 g.) (Found: MeO, 49·8. $C_{10}H_{14}O_3$ requires 3MeO, 51·1%).

1 : 3 : 4-*Trihydroxy-2-methylanthraquinone.* Powdered anhydrous aluminium chloride (2 g.), was added to a mixture of phthalic anhydride (1 g.), 2 : 3 : 6-trimethoxytoluene (2 g.), and carbon disulphide (30 c.c.), and the whole heated under reflux during 24 hours. The carbon disulphide was removed, the residue decomposed with cold dilute hydrochloric acid, and unchanged initial materials removed by distillation in steam. The semi-solid residue was taken up in a large volume of ether, and the solution dried and concentrated; the crude benzoylbenzoic acid separated as yellowish crystals. Recrystallised from ether, it formed colourless prisms, m. p. 205—208° (Found: C, 65·7; H, 5·5. $C_{18}H_{18}O_6$ requires C, 65·5; H, 5·4%). The acid gave no coloration with ferric chloride in alcoholic solution.

The above benzoylbenzoic acid (0·4 g.) was heated with concentrated sulphuric acid (2 c.c.) at 150—160° for 30 minutes. The solution acquired a deep red-violet colour, and on cooling and pouring into water a red-brown precipitate was produced; this was boiled with water for a few minutes to coagulate, collected, washed with hot water, dried, and purified by sublimation in a high vacuum and crystallisation from 96% alcohol. The product (yield, *ca.* 20 mg.) formed red needles, m. p. *ca.* 268—270°, with partial sublimation; it appeared to contain water of crystallisation (Found: C, 62·6; H, 4·4. $C_{15}H_{10}O_5,H_2O$ requires C, 62·5; H, 4·2%).

1 : 3 : 4-*Trihydroxy-2-methylanthraquinone* is readily soluble in aqueous sodium hydroxide or carbonate solution with a bluish-crimson colour. Its solution in concentrated sulphuric acid is bluish-crimson—very reminiscent of purpurin, which it resembles also in the colour of its acetic acid solutions—yellow with but feeble greenish fluorescence. It is, however, a weaker adjective dye than purpurin.

The yield of anthraquinone in this synthesis was poor, since the major part of the crude product was a mixture of colourless prisms and needles. The nature of this acidic substance has not yet been determined.

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20. *The Racemisation of Some* d-o-(2-*Dimethylaminophenyl*)*phenyltrimethylammonium Salts.*

By Dorothy E. Cook and E. E. Turner.

Shaw and Turner (J., 1933, 135) found that in aqueous solution at 99·5° *d*-*o*-(2-dimethylaminophenyl)phenyltrimethylammonium *d*-camphorsulphonate racemised, as regards the cation, rather more quickly than did the corresponding *d*-ammonium iodide. This effect appeared to be most readily explicable as due to electrostriction differences between the two salts. Were this so, the corresponding d-*ammonium benzenesulphonate* should have an optical stability nearer to that of the camphorsulphonate than to that of the iodide. In effecting a comparison of the three salts, we employed solutions of equimolecular concentration, which we had not done previously. At 90°, the periods of half-racemisation were: benzenesulphonate 210 minutes, iodide 250 minutes, and *d*-camphorsulphonate 310 minutes. In equivalent aqueous solutions, therefore, the camphorsulphonate is more stable, but the

benzenesulphonate is less stable, than the iodide, and the cause of the different stabilities is not apparent.

A study has also been made of the racemisation of the above *d*-camphorsulphonate in different solvents at 90°. The following results show that there is no simple connexion between the speed of racemisation and the dielectric constant (μ) of the solvent :

Solvent.	Period of half-racemisation (mins.).	μ.
Water	310	80·0
Ethyl alcohol	300	23·5
Acetone	155	21·4
Acetonitrile	140	38·8
Chloroform	100	5·05

Actually, racemisation was more rapid the higher the solubility of the camphorsulphonate in the solvent.

Determination of the rate of racemisation of the above iodide and *d*-camphorsulphonate in aqueous solutions at 85°, 90° and 95° allowed of the calculation of the activation energy of the process. This was found to be, for the iodide, 11,500 cals., and for the camphorsulphonate, 19,000 cals.

EXPERIMENTAL.

d-o-(2-*Dimethylaminophenyl)phenyltrimethylammonium benzenesulphonate* was prepared from the corresponding iodide and the equivalent amount of silver benzenesulphonate in boiling aqueous alcohol (Found : N, 6·7. $C_{23}H_{28}O_3N_2S$ requires N, 6·7%).

Measurements of the Rates of Racemisation.—These were made by heating a solution of the salt under examination in a sealed glass tube for definite times and at definite temperatures, all usual controls being made use of. The results are tabulated below :

d-o-(2-*Dimethylaminophenyl)phenyltrimethylammonium* d-*camphorsulphonate*. (a) $t = 90°$. (1) Solvent, water; *c*, 0·5268.

Time (mins.).	α_{5791}.	α_{5461}.	*k*.	Time (mins.).	α_{5791}.	α_{5461}.	*k*.
0	+0·50°	+0·58°	—	200	+0·36°	+0·41°	$0·0009_9$
50	0·46	0·53	$0·0009_4$	280	0·32	0·37	$0·0009_5$
90	0·43	0·50	$0·0009_8$	370	0·28	0·31	$0·0010_2$
150	0·39	0·44	$0·0009_7$	∞	0·11	0·12	—

Half-life period 310 mins. Mean *k* $0·0009_8$.

(2) Solvent, ethyl alcohol; *c*, 1·1860. Mean *k*, 0·0010. Limits, $0·0009_9$ and $0·0012_9$. Half-life period, 300 mins.

(3) Solvent, acetone; *c*, 1·3310. Mean *k*, $0·0019_4$. Limits, $0·0018_9$ and 0·0023. Half-life period, 155 mins.

(4) Solvent, acetonitrile; *c*, 1·2950. Mean *k*, $0·0021_4$. Limits, $0·0020_2$ and 0·0024. Half-life period, 140 mins.

(5) Solvent, chloroform; *c*, 1·1370. Mean *k*, 0·003. Half-life period, 100 mins. Solution darkened during measurements.

(b) $t = 85°$. Solvent, water; *c*, 0·5268. Mean *k*, $0·0006_5$. Limits, $0·0006_1$ and $0·0007_0$. Half-life period, 460 mins.

(c) $t = 95°$. Solvent, water; *c*, 0·5268. Mean *k*, $0·0013_3$. Limits, $0·0012_6$ and $0·0013_9$. Half-life period, 230 mins.

d-o-(2-*Dimethylaminophenyl)phenyltrimethylammonium* d-*iodide*. Solvent, water; *c*, 0·4140.
(1) $t = 85°$. Mean *k*, $0·0009_3$. Limits, 0·0009, and $0·0009_7$. Half-life period, 320 mins.
(2) $t = 90°$. Mean *k*, $0·0011_9$. Limits, $0·0011_6$ and $0·0012_5$. Half-life period, 250 mins.
(3) $t = 95°$. Mean *k*, $0·0014_5$. Limits, $0·0013_8$ and $0·0014_6$. Half-life period, 210 mins.

d-o-(2-*Dimethylaminophenyl)phenyltrimethylammonium benzenesulphonate*.
Solvent, water; *c*, 0·4478. Mean *k*, $0·0014_2$. Limits, $0·0014_0$ and $0·0014_8$. Half-life period, 210 mins.

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21. *A Reaction of Certain Diazosulphonates derived from β-Naphthol-1-sulphonic Acid. Part XVII. Conversion of Nitro-3-aryl- and Nitro-3-aryl-4-methyl-phthalaz-1-ones into Corresponding Phthalaz-4-ones by Migration of the Nitroaryl Group, and Related Reactions.*

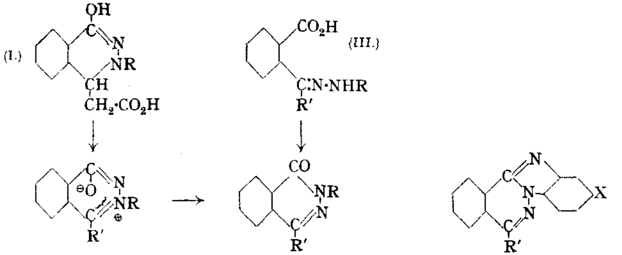
By F. M. Rowe, D. A. W. Adams, A. T. Peters, and (in part) A. E. Gillam.

In Part XI (J., 1933, 1068) it was stated that when 1-hydroxy-3-(4′-nitrophenyl)-3 : 4-dihydrophthalazine-4-acetic acid (I; R = 4′-nitrophenyl) was heated with dilute hydrochloric acid (1 : 7·5) in a sealed tube at 175° for 6 hours, the product appeared to be a mixture of 4′-nitro-3-phenyl- and 4′-nitro-3-phenyl-1-methyl-phthalaz-4-one (IV; R = 4′-nitrophenyl, R′ = H and Me respectively). The latter compounds had been obtained hitherto only by the reaction of *p*-nitrophenylhydrazine with *o*-phthalaldehydic acid (J., 1928, 2555) and with acetophenone-*o*-carboxylic acid (J., 1931, 1923) respectively, since the products of the action of boiling dilute sulphuric acid (J., 1928, 2553) and cold acid dichromate (J., 1931, 1070) respectively on (I; R = 4′-nitrophenyl) are the isomerides 4′-nitro-3-phenyl- and 4′-nitro-3-phenyl-4-methyl-phthalaz-1-one (II; R = 4′-nitrophenyl, R′ = H and Me respectively). The above reaction with dilute hydrochloric acid in a sealed tube therefore indicated not only that nitroarylphthalaz-4-ones could be obtained in a new way, but also that this involved the possibility of converting nitroarylphthalaz-1-ones into the corresponding phthalaz-4-ones. We have now studied these reactions in detail and have established that this type of conversion can be effected readily. In order to avoid confusion, the nomenclature used in previous parts of this series is retained, although it follows from the present investigation that the two series of nitroarylphthalazones are differentiated more clearly and correctly if compounds (IV) are termed nitro-2-aryl- and nitro-2-aryl-4-methyl-phthalaz-1-ones instead of nitro-3-aryl- and nitro-3-aryl-1-methyl-phthalaz-4-ones.

Numerous nitro- and amino-3-arylphthalaz-4-ones, and the corresponding 1-methyl compounds, required for purposes of reference in the present investigation have already been described (J., 1936, 311). It proved desirable, however, to prepare compounds containing a nitro- or an amino-group in the 2′-position and, in doing so, we observed a property peculiar to the 2′-nitro-compounds which made it clear that the substance, pale yellow needles, m. p. 239°, considered to be 2′-amino-3-phenyl-1-methylphthalaz-4-one (*ibid.*, p. 314), is not that compound. The actual colourless 2′-*amino-3-aryl-* and 2′-*amino-3-aryl-*1-*methyl-phthalaz-4-ones* (IV; R = 2′-aminoaryl, R′ = H and Me respectively) are obtained satisfactorily only from the corresponding *o*-carboxy-benzaldehyde- and -acetophenone-2′-nitroarylhydrazones (III; R′ = H and Me respectively) with aqueous sodium sulphide, which effects both ring closure and reduction, whereas yellow substances with different properties are the main products of reducing (IV; R = 2′-nitroaryl, R′ = H or Me) with aqueous-alcoholic sodium sulphide. The amino-compounds (IV) readily form *acetyl* derivatives, are diazotisable and couple to form azo-dyes, and, when heated with dilute hydrochloric acid (1 : 8) in a sealed tube at 180° for 6 hours, are converted almost quantitatively into the basic 2′ : 4-*anhydro*-derivatives (V; R′ = H or Me). On the other hand, the yellow substances yield only traces of the acetyl derivative of (IV) (possibly derived from a little of the amino-compound that may be present), are not diazotisable, and are not convertible into (V). Owing to the fact that variable analyses are obtained according to the conditions used in crystallisation and drying, the yellow substances were not examined further, but they may well be intermediate hydroxylamine derivatives which cannot be reduced to the amino-compounds.

The study of the influence of variations in the conditions on the conversion of (II; R = nitroaryl, R′ = H or Me) into (IV; R = nitroaryl, R′ = H or Me) is facilitated by the great differences in properties between the two types of compound, by means of which mixtures are separated with exceptional ease. Compounds (II) are both acidic and basic; in many cases they form readily soluble hydrochlorides, and all dissolve readily in aqueous sodium hydroxide, but are practically insoluble in such hydrocarbon solvents as benzene

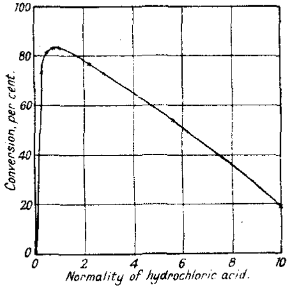
and toluene. On the other hand, compounds (IV) are insoluble in aqueous mineral acids and alkalis, but are readily soluble in hydrocarbon solvents.



(II.) (IV.) (V; R′ = H or Me; X = H, Me, or Cl.)

In general, nitro-3-arylphthalaz-1-ones (II; R′ = H) and the corresponding 4-methyl compounds (II; R′ = Me) are best converted into nitro-3-arylphthalaz-4-ones (IV; R′ = H) and the corresponding 1-methyl compounds (IV; R′ = Me), respectively, by heating with dilute hydrochloric acid in a sealed tube at temperatures between 170° and 190° for 6 hours; temperatures above 190° usually result in some decomposition and the product is charred. Under similar conditions, the conversion is also brought about by dilute sulphuric acid, as well as by dilute acetic acid to a less extent, but water alone and aqueous alkalis are ineffective. The ratio of the weight of (II; R′ = H or Me) to the volume of dilute hydrochloric acid appears to be of little importance, but with tubes of the capacity that we employed 1—1·5 g. of (II) to 18 c.c. acid is most satisfactory. The strength of the acid used, however, has a marked effect on the rate and extent of conversion, as is illustrated by Fig. 1, which shows the percentage yield of (IV) obtained when (II; R = 4′-nitrophenyl, R′ = Me) (1 g.) is heated with dilute hydrochloric acid (18 c.c.; various strengths) at 180° for 6 hours.

Fig. 1.



This conversion proceeds most readily when approximately 1·2*N*-hydrochloric acid is used, and we employed acid of this strength generally throughout the investigation. In most cases, the conversion is neat at an appropriate temperature, being unaccompanied by any side reaction, and usually it is possible to account for 90—95% of (II) by recovering unaltered material. The temperature employed is very important in certain cases, because with (II; R = 2′-nitroaryl, or 2′-halogeno- or 2′ : 6′-dihalogeno-4′-nitrophenyl, R′ = Me), although compounds (IV; R′ = Me) are obtained at a suitably high temperature, different compounds (VI) (see p. 93) are produced at a lower temperature. On the other hand, compound (II; R = 4′-nitrophenyl, R′ = Me) is converted into the corresponding compound (IV) to some extent even by refluxing with dilute hydrochloric acid.

The results for the conversion of (II; R = 4′-nitrophenyl, R′ = Me) into (IV; R = 4′-nitrophenyl, R′ = Me) by heating with dilute hydrochloric acid in a sealed tube at 180° for various times (see p. 99) indicate that the reaction approximately follows a unimolecular course, the average value of k being 48×10^{-4}.

The ease of conversion of (II; R = nitroaryl, R′ = H or Me) into the corresponding compound (IV) varies considerably with the nature and position of substituents in the

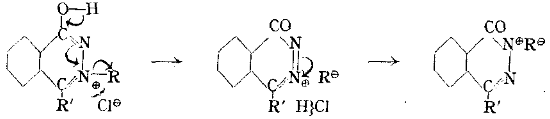
3-phenyl nucleus, as is illustrated in the table, where the percentage conversion is tha obtained after heating for 6 hours.

	R′ = H.		R′ = Me.	
R.	% Conversion.	$k \times 10^4$.	% Conversion.	$k \times 10^4$.
4′-Nitrophenyl	66	30	82	48
4′-Nitro-2′-methylphenyl	20	5	27	9
2′-Chloro-4′-nitrophenyl	—	—	49	19
2′-Bromo-4′-nitrophenyl	—	—	27	9
2′ : 6′-Dichloro-4′-nitrophenyl	46	17	17	4·5
2′ : 6′-Dibromo-4′-nitrophenyl	20 *	3	—	—
3′-Nitrophenyl	14	4	25	8
2′-Nitrophenyl	—	—	65	30
2′-Nitro-4′-methylphenyl	36	12	53	21
4′-Chloro-2′-nitrophenyl	68	32	74	37

* After heating for 10 hours.

The figures given for (R = 2′-nitroaryl or halogeno-4′-nitrophenyl, R′ = Me) do not strictly indicate the velocity of conversion of (II) into (IV), because in these cases there is certainly formation of some of the corresponding compound (VI) during preliminary heating, although at the temperatures ultimately attained in the above experiments, (VI) is converted into (IV). The fact that (R = 2′ : 6′-dichloro-4′-nitrophenyl, R′ = Me) is the only example amongst those examined where the yield of (IV) is less than is the case with the analogous lower homologue (R′ = H), is due to the necessity for an abnormally high temperature of conversion with the former in order to avoid formation of the corresponding compound (VI). Compounds (II) containing a nitro-group in the *o*- or the *p*-position of the 3-phenyl nucleus are converted into (IV) much more readily than is the case when the nitro-group is in the *m*-position, halogen in the *o*-position reduces the rate of conversion considerably, the retarding influence of bromine being much greater than that of chlorine, and a methyl group in either the *o*- or the *p*-position also has a notable retarding effect.

The following mechanism, involving migration of the nitroaryl group, is suggested for the conversion of compounds (II; R′ = H or Me) into (IV; R′ = H or Me). The nitroaryl group (R) is considered to migrate, with its pair of binding electrons, as an anion. Thus, the first stage is an electronic redistribution in the hydrochloride of the nitro-3-arylphthalaz-1-one (II*a*; R′ = H or Me), promoted by the electron-attracting group (R), leading to the separation of the latter as an anion (II*b*). A further redistribution of electrons then occurs (II*c*), followed by the reattachment of the anionic group (R) at the 2-nitrogen atom with formation of (IV; R′ = H or Me).



(II*a*.) (II*b*.) (II*c*.)

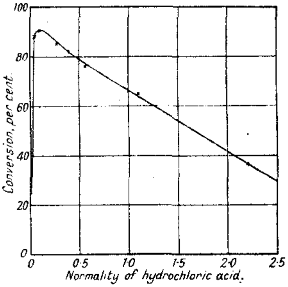
The actual velocity of the conversion is governed by the ease of separation of the nitroaryl group (R), the succeeding changes being so rapid as to be incapable of measurement. Thus, although the group (R) is shown in (II*b*) as a free ion, it is considered to be captured immediately by the positive 2-nitrogen atom (II*c*) before it can escape into the bulk of the reaction mixture. Such a mechanism closely resembles that suggested by Stevens and co-workers for the rearrangement of phenacyl- and acetonyl-benzyldimethylammonium salts (*J.*, 1928, 3193; 1930, 2107, 2119; 1932, 55, 1926), and is preferred to the alternative type of mechanism in which the migrating aryl group is considered to attract one or both of the lone pair of electrons on the nitrogen atom to which it is migrating (cf. the conversion of *N*-phenylbenziminophenyl ethers into benzoyldiphenylamines, and the reversible rearrangement of triarylbenzenylamidines: Chapman, J., 1925, **127**, 1992; 1927, **1743**; 1929, 2133; 1930, 2462; 1932, 1770; see also Bennett, *Ann. Reports*, 1929, **26**, 123).

The literature, however, appears to contain no example of the migration of an aryl group from one nitrogen atom to another nitrogen atom in a ring, as occurs in our case.

That our reaction is intramolecular in character and does not involve the presence of free ions, is clear from the fact that when a mixture of equal quantities of (II; R = 4'-nitrophenyl, R' = Me) and (II; R = 2' : 6'-dichloro-4'-nitrophenyl, R' = H) is heated under conditions suitable for conversion, only (IV; R = 4'-nitrophenyl, R' = Me) and (IV; R = 2' : 6'-dichloro-4'-nitrophenyl, R' = H) are obtained. If free ions were actually present at any stage during the conversion, the reaction product would be expected to contain also (IV; R = 4'-nitrophenyl, R' = H) and (IV; R = 2' : 6'-dichloro-4'-nitrophenyl, R' = Me), but no trace of these two compounds could be detected.

It has already been mentioned that certain nitro-3-aryl-4-methylphthalaz-1-ones (II; R' = Me) give a different product when heated with dilute hydrochloric acid at a temperature lower than that required for conversion into (IV; R' = Me). This novel reaction proceeds most readily with (II; R = 2'-nitroaryl, R' = Me), in which case the conversion is best effected by refluxing with dilute hydrochloric acid and 2-(2'-*nitroarylamino*)-3-*methylene*iso*indolinone* (VI; R = 2'-nitroaryl) separates progressively in yellow needles. Compounds (VI) are of a new type in these investigations, isomeric with the corresponding compounds (II; R' = Me) and (IV; R' = Me), and are insoluble in both dilute mineral acids and aqueous alkalis. In agreement with the constitution proposed, they are hydrolysed by boiling alcoholic sodium ethoxide with formation of the corresponding *o*-carboxyacetophenone-2'-nitroarylhydrazones (III; R' = Me), and are oxidised by chromic acid to the corresponding N-2'-*nitroarylaminophthalimides* (named phthalyl-2'-nitroarylhydrazides in J., 1935, 1808). The product of their reduction varies with the reagent used, boiling aqueous-alcoholic sodium sulphide producing the corresponding 2'-amino-3-aryl-1-methylphthalaz-4-ones (IV; R = 2'-aminoaryl, R' = Me), and iron powder and acetic acid the 2-(2'-*aminoarylamino*)-3-*methylene*iso*indolinones* (VI; R = 2'-aminoaryl).

Fig. 2.



It is noteworthy that in the latter case the C:CH_2 linkage is *not* reduced with formation of 2-(2'-aminoarylamino)-3-methyl*iso*indolinone. This stability of the methylene group is further exemplified by the facts that compounds (VI; R = 2'-nitroaryl) do not react with bromine water, or form perchlorates, or react in the ways that 1-methoxy-3-(4'- and 3'-nitroaryl)-4-methylene-3 : 4-dihydrophthalazines do (cf. J., 1936, 1704), although an intense violet colour is produced when (VI; R = 2'-nitrophenyl) is boiled with *p*-dimethylaminobenzaldehyde in acetic anhydride solution in presence of a little sulphuric acid. Finally, compounds (VI; R = 2'-nitroaryl) are converted into the corresponding 2'-nitro-3-aryl-1-methylphthalaz-4-one (IV; R' = Me) by heating with dilute hydrochloric acid (1 : 8) in a sealed tube at 180—190° for 6 hours, or much more readily by heating a solution in concentrated sulphuric acid at 180° for 1—2 minutes. As fuming sulphuric acid is equally effective in the latter method, it is clear that this conversion of (VI; R = 2'-nitroaryl) into (IV; R = 2'-nitroaryl, R' = Me) does not involve the addition and subsequent removal of the elements of water. Compounds (VI; R = 2'-nitroaryl) cannot be synthesised, because methylenephthalide (Gabriel, *Ber.*, 1884, **17**, 2521) does not react with an *o*-nitroarylhydrazine in boiling alcoholic or glacial acetic acid solution, and when a mixture of the two is heated at 120° the product is (III; R = 2'-nitroaryl, R' = Me).

The conversion of (II; R = 2'-nitroaryl, R' = Me) into (VI; R = 2'-nitroaryl) is influenced considerably by the strength of the acid employed, as is illustrated by Fig. 2, which shows the percentage yield of (VI) obtained when (II; R = 2'-nitrophenyl, R' = Me)

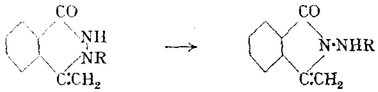
(1·5 g.) is heated with dilute hydrochloric acid (18 c.c.; various strengths) in a sealed tube at 150° for 6 hours.

Under these conditions, water alone effects this conversion to a moderate extent, but the maximum yield of (VI) is obtained when approximately 0·1—0·2*N*-hydrochloric acid is used. As already stated, with (II; R = 2′-nitroaryl, R′ = Me) this conversion is best carried out by refluxing with dilute hydrochloric acid, in which case the maximum effect is produced by somewhat stronger acid than when a sealed tube is employed. The results for the conversion of (II; R = 2′-nitrophenyl, R′ = Me) into the corresponding compound (VI) by refluxing with 0·8*N*-hydrochloric acid for various times (see p. 102) indicate that the reaction approximately follows the unimolecular law, the average value of *k* being 41×10^{-3}.

The only compounds other than (II; R = 2′-nitroaryl, R′ = Me) that we have succeeded in converting into the corresponding compounds (VI) are (II; R = 2′-halogeno-4′-nitro- or 2′ : 6′-dihalogeno-4′-nitro-phenyl, R′ = Me). With these 4′-nitro-compounds, however, the reaction occurs much less readily; for instance, refluxing with dilute hydrochloric acid is ineffective, and heating with dilute hydrochloric acid in a sealed tube at 160—165° for 6 hours is necessary in order to obtain the 2-(2′-*halogeno*-4′-*nitro*- and 2′ : 6′-*dihalogeno*-4′-*nitro-phenylamino*)-3-*methylene*iso*indolinone* (VI). The latter compounds possess similar properties and undergo similar reactions to those already outlined for their 2′-nitro-analogues.

The ease of conversion of (II; R = nitroaryl, R′ = Me) into the corresponding compounds (VI; R = nitroaryl) varies considerably with the nature and position of substituents in the 3-phenyl nucleus, and the reaction velocities in the cases which we have studied are in the order R = 4′-chloro-2′-nitrophenyl > 2′-nitrophenyl > 2′-nitro-4′-methylphenyl ≫ 2′-chloro-4′-nitrophenyl > 2′-bromo-4′-nitrophenyl > 2′ : 6′-dichloro-4′-nitrophenyl > 2′ : 6′-dibromo-4′-nitrophenyl.

The rearrangement of (II) to (VI), although also intramolecular in character, is probably entirely different in mechanism from that suggested for the conversion of (II) into (IV), and merely involves a change of linkage in the tautomeric methylene form (II*d*) of (II; R′ = Me).

(II*d*.)  (VI.)

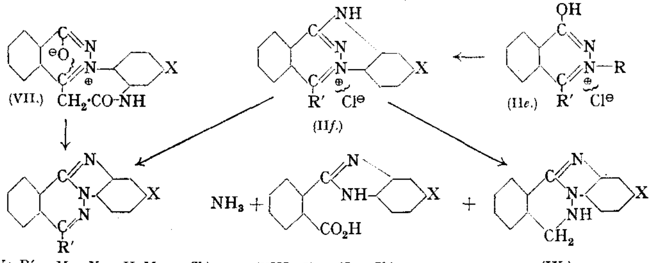
It is considered to be most improbable that the conversion of nitro-3-aryl-4-methylphthalaz-1-ones (II; R′ = Me) into nitro-3-aryl-1-methylphthalaz-4-ones (IV; R′ = Me) involves the intermediate formation of the corresponding compound (VI), because there is no evidence of the formation of (VI; R = 3′- or 4′-nitrophenyl); moreover it is impossible to obtain analogues of (VI) from (II; R = nitroaryl, R′ = H), yet the latter are convertible into (IV; R = nitroaryl, R′ = H).

p- and *m*-Amino-3-phenylphthalaz-1-ones (II; R = 4′- or 3′-aminophenyl, R′ = H) and the corresponding 4-methyl compounds cannot be converted into the amino-derivatives of the respective 4-ones (IV; R = 4′- or 3′-aminophenyl, R′ = H or Me), but are recovered unaltered after heating with dilute hydrochloric acid in a sealed tube. This supports the mechanism suggested for the conversion of (II; R = nitroaryl, R′ = H or Me) into (IV; R = nitroaryl, R′ = H or Me), because the amino-group is capable of electron release, and it is improbable that the positive ammonium group, which would promote the reaction, would be formed under the conditions employed.

o-Amino-3-arylphthalaz-1-ones (II; R = 2′-aminoaryl, R′ = H) and the corresponding 4-methyl compounds (II; R = 2′-aminoaryl, R′ = Me), however, do react when heated with dilute hydrochloric acid (1 : 8) in a sealed tube at 180° for 6 hours, although in quite unexpected ways. These new reactions take an entirely different course with (II; R′ = Me) from that with (II; R′ = H). Thus, 2′-amino-3-aryl-4-methylphthalaz-1-ones (II; R = 2′-aminoaryl, R′ = Me) or 2′-amino-3-arylphthalaz-1-one-4-acetic acid lactams

(VII) are converted into 2′ : 4-anhydro-2′-amino-3-aryl-1-methylphthalaz-4-ones (V; R′ = Me), identical with the compounds already obtained under the same conditions from (IV; R = 2′-aminoaryl, R′ = Me), although the yield is not as good as in the latter case. On the other hand, with (II; R = 4′-chloro-2′-aminophenyl, R′ = H) the 2-nitrogen atom is eliminated as ammonia, and 5-chloro-2-phenylbenziminazole-*o*-carboxylic acid (VIII; X = Cl) and 5-chloro-*o*-benzylenebenziminazole (IX; X = Cl) (cf. J., 1935, 1798) are obtained. The sulphate of the substance which possesses the properties of 2′-amino-3-phenylphthalaz-1-one (*loc. cit.*) behaves similarly, and is converted into ammonia, 2-phenylbenziminazole-*o*-carboxylic acid, and *o*-benzylenebenziminazole. In this remarkable reaction, as the 2-nitrogen atom is eliminated by reduction to ammonia, naturally the oxidation product (VIII) is formed in much greater quantity than the reduction product (IX).

In view of the non-reactivity of the 4′- and 3′-amino-analogues, the first stage of these reactions with both (II; R = 2′-aminoaryl, R′ = H) and (II; R = 2′-aminoaryl, R′ = Me) is almost certainly the removal of 1 molecule of water from the 2′-amino- and the 1-hydroxyl group of the hydrochloride (II*e*). The resulting (II*f*; R′ = H) is so unstable that it decomposes immediately with elimination of the 2-nitrogen atom as ammonia, whilst most of the residue is oxidised to (VIII) and the remainder is reduced to (IX). The corresponding (II*f*; R′ = Me) is rather more stable owing to the presence of the 4-methyl group, which can react in the methylene form, and so only rearrangement occurs with formation of (V; R′ = Me). This rearrangement may take place by a mechanism essentially similar to that suggested for the conversion of (II; R = nitroaryl, R′ = H or Me) into (IV; R = nitroaryl, R′ = H or Me), or merely by change of linkage in (II*f*) resulting in the formation of the hydrochloride of (V).



The reactivity of the 2′-amino-group is further illustrated, and an additional relationship of the compounds under discussion established, by the fact that (VI; R = 2′-aminophenyl) is readily converted into (V; R′ = Me, X = H) by heating with dilute hydrochloric acid (1 : 8) in a sealed tube at 180° for 6 hours. In this case it is improbable that the 2′-amino-group and the 1-keto-group of (VI) would react with removal of 1 molecule of water. Consequently, the first stage in this conversion is more likely to be an intramolecular rearrangement with formation of (IV; R = 2′-aminophenyl, R′ = Me), followed by removal of 1 molecule of water from the latter: the ease with which (VI; R = nitroaryl) is converted into (IV; R = nitroaryl, R′ = Me) tends to support this view.

We have fully confirmed the suggestion that the product of heating (I; R = 4′-nitrophenyl) with dilute hydrochloric acid (1 : 7·5) in a sealed tube at 175° for 6 hours is a mixture of (IV; R = 4′-nitrophenyl, R′ = H) and (IV; R = 4′-nitrophenyl, R′ = Me) (J., 1933, 1068) [compare Bucherer and Fröhlich (*J. pr. Chem.*, 1931, 132, 87), who considered this reaction to be mere decarboxylation of (I)]. These two compounds are formed in a ratio of approximately 45 : 55, and, although they cannot be separated by fractional crystallisation, after reduction of the mixture of nitro-compounds, some (IV; R = 4′-

aminophenyl, R′ = Me) can be isolated by fractional crystallisation of the mixed amino-compounds. This proof of the presence of (IV; R = 4′-nitrophenyl, R′ = Me) in the product under these conditions is of interest, because the sole product of heating (I; R = 4′-nitrophenyl) with dilute hydrochloric acid (1 : 2) in a sealed tube, or of refluxing it with dilute sulphuric acid, is (II; R = 4′-nitrophenyl, R′ = H). On the other hand, when (I; R = 3′-nitrophenyl) is heated with dilute hydrochloric acid (1 : 7·5) under the same conditions as the 4′-nitro-isomeride, the product is (II; R = 3′-nitrophenyl, R′ = H), some of which is converted into (IV; R = 3′-nitrophenyl, R′ = H) by prolonging the period of heating, but none of the corresponding methyl compounds (II or IV; R′ = Me) could be detected. Compound (I; R = 2′-nitrophenyl), however, behaves similarly to the 4′-nitro-isomeride, except that it is necessary to heat at 190—195°; the product is a mixture of (IV; R = 2′-nitrophenyl, R′ = H) and (IV; R = 2′-nitrophenyl, R′ = Me) in which the latter predominates.

When (I; R = 4′-aminophenyl) is heated with dilute hydrochloric acid in a sealed tube, the sole product is (II; R = 4′-aminophenyl, R′ = H), but the behaviour of (I; R = 2′-aminophenyl) is entirely different. In the latter case, the reaction probably proceeds *via* (II; R = 2′-aminophenyl, R′ = H) and (II; R = 2′-aminophenyl, R′ = Me), for the products are ammonia, 2-phenylbenziminazole-*o*-carboxylic acid (VIII; X = H), and 2′ : 4-anhydro-2′-amino-3-phenyl-1-methylphthalaz-4-one (V; R′ = Me, X = H). No doubt, *o*-benzylenebenziminazole (IX; X = H) also is formed to a small extent and in this case is lost during the crystallisation of (V).

EXPERIMENTAL.

o-*Carboxybenzaldehyde-2′-nitroarylhydrazones* (III; R′ = H).—These compounds (or their lactone forms) were prepared as described for their analogues (J., 1928, 2555; 1936, 312).

Methods of converting (III) *into 2′-Nitro-3-arylphthalaz-4-ones* (IV; R′ = H).—In all cases 0·5 g. of (III) was used. (i) Heating at 20° below the m. p. of the corresponding compound (IV) for 15 minutes; refluxing with (ii) alcohol (10 c.c.) for 1 hour, or (iii) glacial acetic acid (5 c.c.) for 20 minutes, or (iv) nitrobenzene (5 c.c.) for 1 hour, or (v) acetic anhydride (5 c.c.) for ½ hour, or (vi) acetic anhydride (5 c.c.) and pyridine (3 drops) for 3 hours; (vii) dissolution in cold concentrated sulphuric acid (10 c.c.), the solution being left over-night. Any unchanged (III) was extracted with alkali.

2′-Amino-3-arylphthalaz-4-ones (IV; R′ = H, R = 2′-aminoaryl).—These compounds were made only from (III) [method (a)], as reduction of (IV; R = 2′-nitroaryl) gave yellow substances [method (b)] with different properties. (a) A suspension of (III) (5 g.) in water (100 c.c.) was heated with sodium sulphide crystals (50 g.) in water (50 c.c.) at 50—60° until the bluish-red colour of the solution changed to orange-yellow, and almost colourless crystals had separated. (b) Finely divided (IV) (5 g.) was refluxed with a solution of sodium sulphide crystals (50 g.) in water (125 c.c.) and alcohol (125 c.c.) until the red colour of the solution changed to orange and yellow needles had separated.

2′ : 4-Anhydro-2′-amino-3-arylphthalaz-4-ones (V; R′ = H).—These compounds were prepared by heating (IV; R′ = H, R = 2′-aminoaryl) (1 g.) with dilute hydrochloric acid (18 c.c.; 1 : 8) in a sealed tube at 180° for 6 hours. The reaction mixture was either a colourless solution or a suspension of colourless needles of the hydrochloride and was neutralised with aqueous sodium hydroxide.

Reduction of (III *and* IV; R = *2′-Nitrophenyl*).—(a) 2′-Amino-3-phenylphthalaz-4-one (*J.*, 1936, 312). (b) The *substance* crystallised from alcohol in bright yellow needles, m. p. 248° (yield, 3·2 g.) (Found: C, 66·55; H, 4·6; N, 16·55. $C_{14}H_{11}O_2N_3$ requires C, 66·4; H, 4·35; N, 16·6%).

2′ : 4-Anhydro-2′-amino-3-phenylphthalaz-4-one crystallised from methyl alcohol in colourless needles, m. p. 178° (yield 0·9 g.; 97·4%) (Found: C, 76·4; H, 4·5; N, 18·7. $C_{14}H_9N_3$ requires C, 76·7; H, 4·1; N, 19·2%), readily soluble in dilute mineral acids, but insoluble in aqueous alkalis.

m-*Nitro*-p-*tolylhydrazine*.—The following method of preparation gave better results than that described by Davies (J., 1922, 121, 720). A fine suspension of *m*-nitro-*p*-toluidine (18 g.) in concentrated hydrochloric acid (160 c.c.) and water (50 c.c.) was diazotised at 0° with sodium nitrite (8·5 g.) in water (25 c.c.), and the excess of nitrous acid was destroyed with urea. The filtered cold diazo-solution was added during 1 hour with good agitation to a solution of stannous

chloride (45 g.) in concentrated hydrochloric acid (60 c.c.) at – 14°, the precipitate filtered off and dissolved in boiling water (300 c.c.) (charcoal), and tin removed with hydrogen sulphide. After boiling, sodium chloride was added until the hydrochloride began to separate in yellow needles, which were collected and dissolved in water, and the base liberated at 60° by addition of sodium acetate. *m*-Nitro-*p*-tolylhydrazine crystallised from alcohol in bright red needles, m. p. 112° (yield, 10·8 g.; 54·6%) (Davies, *loc. cit.*, gives m. p. 110°).

(III; R = 2'-*Nitro*-4'-*methylphenyl*) crystallised from alcohol in bright red needles, m. p. 228° (refluxed for 10 minutes; yield, 90·2%) (Found: N, 14·4. $C_{15}H_{13}O_4N_3$ requires N, 14·05%), soluble in sodium carbonate and hydroxide solutions with orange-red and bluish-red colours, respectively. Conversion into (IV; R = 2'-nitro-4'-methylphenyl): Methods (i) to (iv) nil; (v) and (vi) complete; (vii) 92%.

(IV; R = 2'-*Nitro*-4'-*methylphenyl*) crystallised from glacial acetic acid in large, almost colourless prisms, m. p. 195° (Found: C, 64·15; H, 3·85; N, 15·1. $C_{15}H_{11}O_3N_3$ requires C, 64·1; H, 3·9; N, 14·95%), insoluble in aqueous alkalis and hydrochloric acid. This compound and the 4'-chloro-analogue described below were best prepared by method (vii).

Reduction of (III *and* IV; R = 2'-*Nitro*-4'-*methylphenyl*).—(a) An intractable tar was obtained on concentrating the reaction mixture. (b) The *substance* crystallised from alcohol in bright yellow needles (3 g.), m. p. 216° (Found: C, 65·4; H, 4·7; N, 15·6. $C_{15}H_{13}O_2N_3$ requires C, 67·4; H, 4·85; N, 15·7%). The *acetyl* derivative crystallised from alcohol in colourless needles, m. p. 190° (Found: N, 14·25. $C_{17}H_{15}O_3N_3$ requires N, 14·3%), but the 2' : 4-anhydro-derivative was not prepared, as all attempts to obtain it from the yellow compound were unsuccessful.

4-*Chloro*-2-*nitrophenylhydrazine*.—This compound, prepared from 4-chloro-2-nitroaniline (20 g.) as described above for the 4-methyl analogue, crystallised from alcohol in dark brownish-red needles, m. p. 137° (yield, 11·6 g.; 53·4%); the results were better than those obtained with the method of Plant and Rosser (J., 1928, 2462), who give m. p. 134°.

(III; R = 4'-*Chloro*-2'-*nitrophenyl*) crystallised from alcohol in bright red needles, m. p. 237° (refluxing was unnecessary; yield, 90%) (Found: N, 13·0. $C_{14}H_{10}O_4N_3Cl$ requires N, 13·1%), soluble in sodium carbonate and hydroxide solutions with orange-red and purple colours, respectively. Conversion into (IV; R = 4'-chloro-2'-nitrophenyl): Methods (i) to (iv) nil; (v) 97%; (vi) complete; (vii) 89%.

(IV; R = 4'-*Chloro*-2'-*nitrophenyl*) crystallised from glacial acetic acid in colourless, prismatic needles, m. p. 213—214° (Found: C, 55·9; H, 2·8; N, 13·8; Cl, 11·75. $C_{14}H_8O_3N_3Cl$ requires C, 55·7; H, 2·65; N, 13·9; Cl, 11·8%).

Reduction of (III *and* IV; R = 4'-*Chloro*-2'-*nitrophenyl*).—(a) 4'-*Chloro*-2'-*amino*-3-*phenylphthalaz*-4-*one* crystallised from alcohol in long, colourless needles, m. p. 236° (yield, 3·5 g.; 82·4%) (Found: N, 15·2; Cl, 12·8. $C_{14}H_{10}ON_3Cl$ requires N, 15·45; Cl, 13·1%); the *acetyl* derivative crystallised from alcohol in colourless needles, m. p. 289° (Found: N, 13·1. $C_{16}H_{12}O_2N_3Cl$ requires N,13·4%). (b) The *substance* crystallised from alcohol in yellow needles, m. p. 239° (yield, 3·3 g.) (Found: C, 60·05; H, 3·75; N, 14·95; Cl, 12·6. $C_{14}H_{10}O_2N_3Cl$ requires C, 58·4; H, 3·5; N, 14·6; Cl, 12·3%).

2' : 4-*Anhydro*-4'-*chloro*-2'-*amino*-3-*phenylphthalaz*-4-*one* crystallised from methyl alcohol in long, colourless, feathery needles, m. p. 230° (yield, 0·9 g.; 96·4%) (Found: C, 66·35; H, 3·5; N, 16·9; Cl, 14·2. $C_{14}H_8N_3Cl$ requires C, 66·3; H, 3·15; N, 16·6; Cl, 14·0%).

o-*Carboxyacetophenone*-2'-*nitroarylhydrazones* (III; R' = Me).—These compounds (or their lactone forms) were prepared as described for their analogues (cf. J., 1931, 1923; 1936, 313).

Conversion of (III) *into* 2'-*Nitro*-3-*aryl*-1-*methylphthalaz*-4-*ones* (IV; R' = Me).—Methods (i) to (vii) as described for the unmethylated compounds (p. 96) were used.

2'-*Amino*-3-*aryl*-1-*methylphthalaz*-4-*ones* (IV; R' = Me, R = 2'-aminoaryl).—These compounds were made only from (III) as described for the unmethylated compounds [method (a)] (*loc. cit.*), for reduction of (IV; R = 2'-nitroaryl) gave yellow substances [method (b)] (*loc. cit.*) with different properties.

2' : 4-*Anhydro*-2'-*amino*-3-*aryl*-1-*methylphthalaz*-4-*ones* (V; R' = Me).—These were prepared as described for the unmethylated compounds (*loc. cit.*).

Reduction of (III *and* IV; R = 2'-*Nitrophenyl*).—(a) 2'-*Amino*-3-*phenyl*-1-*methylphthalaz*-4-*one* crystallised from alcohol in colourless needles, m. p. 241° (yield, 3 g.; 71·5%) (Found: C, 71·6; H, 5·4; N, 16·6. $C_{15}H_{13}ON_3$ requires C, 71·7; H, 5·2; N, 16·7%). (b) The *substance* crystallised from alcohol in yellow needles, m. p. 239° (cf. J., 1936, 314) (Found in material crystallised from alcohol and dried at 100° for 1 hour: C, 67·7; H, 5·0; N, 16·25. Found in

material crystallised from pyridine and dried at 130° for 2 hours: C, 72·1; H, 4·6; N, 16·95. $C_{15}H_{13}O_2N_3$ requires C, 67·4; H, 4·85; N, 15·7%).

2' : 4-Anhydro-2'-amino-3-phenyl-1-methylphthalaz-4-one crystallised from aqueous alcohol in colourless, feathery needles, m. p. 163° (yield, 0·9 g.; 97%) (Found: C, 76·8; H, 4·75; N, 18·3. $C_{15}H_{11}N_3$ requires C, 77·25; H, 4·7; N, 18·0%), readily soluble in dilute mineral acids, but insoluble in aqueous alkalis.

(III; R = *2'-Nitro-4'-methylphenyl*) crystallised from alcohol in orange, feathery needles, m. p. 175°, resolidifying and melting again at 256—257° owing to formation of (IV; R = 2'-nitro-4'-methylphenyl) (refluxed for 10 minutes; yield, 90·6%) (Found: N, 13·85. $C_{16}H_{15}O_4N_3$ requires N, 13·4%); it was soluble in aqueous sodium carbonate and hydroxide solutions with orange-red and bluish-red colours, respectively. Conversion into (IV; R = 2'-nitro-4'-methylphenyl): Methods (i) complete; (ii) nil; (iii) 74%; (iv) to (vii) complete.

(IV; R = *2'-Nitro-4'-methylphenyl*) crystallised from glacial acetic acid in colourless prisms, m. p. 258° (Found: C, 65·1; H, 4·4; N, 14·15. $C_{16}H_{13}O_3N_3$ requires C, 65·1; H, 4·4; N, 14·2%), insoluble in aqueous alkalis and hydrochloric acid. This compound and the 4'-chloro-analogue described below were best prepared by method (vii).

Reduction of (III *and* IV; R = *2'-Nitro-4'-methylphenyl*).—(a) *2'-Amino-3-phenyl-1 : 4'-dimethylphthalaz-4-one* crystallised from alcohol in colourless needles, m. p. 203° (yield, 3·5 g.; 82·7%) (Found: C, 72·25; H, 5·7; N, 15·9. $C_{16}H_{15}ON_3$ requires C, 72·45; H, 5·65; N, 15·85%); the *acetyl* derivative crystallised from alcohol in colourless needles, m. p. 263° (Found: C, 70·1; H, 5·95; N, 14·1. $C_{18}H_{17}O_2N_3$ requires C, 70·35; H, 5·55; N, 13·7%). (b) The *substance* crystallised from alcohol in bright yellow needles, m. p. 264—265° (yield, 2·75 g.) (Found: C, 70·2; H, 5·55; N, 15·4. $C_{16}H_{15}O_2N_3$ requires C, 68·3; H, 5·3; N, 14·95%). After concentration of the filtrate, colourless needles, m. p. and mixed m. p. with the amino-compound from method (a) 203° (yield, 0·7 g.; 16·5%), were obtained.

2' : 4-Anhydro-2'-amino-3-phenyl-1 : 4'-dimethylphthalaz-4-one crystallised from aqueous alcohol in pale cream-coloured, feathery needles, m. p. 186° (yield, 0·9 g.; 96·5%) (Found: C, 77·7; H, 5·2; N, 17·3. $C_{16}H_{13}N_3$ requires C, 77·7; H, 5·25; N, 17·0%).

(III; R = *4'-Chloro-2'-nitrophenyl*) crystallised from alcohol in orange, feathery needles, m. p. 185—186° (refluxing was unnecessary; yield, 95%) (Found: N, 12·4. $C_{15}H_{12}O_4N_3Cl$ requires N, 12·6%), soluble in sodium carbonate and hydroxide solutions with orange-red and purple colours, respectively. Conversion into (IV; R = 4'-chloro-2'-nitrophenyl): Methods (i) complete; (ii) nil; (iii) 70%; (iv) to (vii) complete.

(IV; R = *4'-Chloro-2'-nitrophenyl*) crystallised from glacial acetic acid in colourless prisms, m. p. 261° (Found: C, 57·35; H, 3·3; N, 13·1; Cl, 11·5. $C_{15}H_{10}O_3N_3Cl$ requires C, 57·05; H, 3·15; N, 13·3; Cl, 11·25%).

Reduction of (III *and* IV; R = *4'-Chloro-2'-nitrophenyl*).—(a) *4'-Chloro-2'-amino-3-phenyl-1-methylphthalaz-4-one* crystallised from alcohol in colourless needles, m. p. 222—223° (yield, 3·8 g.; 88·7%) (Found: C, 63·5; H, 4·6; N, 15·0; Cl, 12·3. $C_{15}H_{12}ON_3Cl$ requires C, 63·05; H, 4·2; N, 14·7; Cl, 12·4%); the *acetyl* derivative crystallised from alcohol in colourless needles, m. p. 304° (Found: N, 12·85. $C_{17}H_{14}O_2N_3Cl$ requires N, 12·8%). (b) The *substance* crystallised from alcohol in yellow needles, m. p. 212° (yield, 2·7 g.) (Found: C, 61·2; H, 4·35; N, 14·25; Cl, 11·85. $C_{15}H_{12}O_2N_3Cl$ requires C, 59·7; H, 4·0; N, 13·9; Cl, 11·8%).

2' : 4-Anhydro-4'-chloro-2'-amino-3-phenyl-1-methylphthalaz-4-one crystallised from dilute acetic acid in long, colourless, silky needles, m. p. 193° (yield, 0·9 g.; 96%) (Found: C, 67·4; H, 4·0; N, 16·1; Cl, 13·5. $C_{15}H_{10}N_3Cl$ requires C, 67·3; H, 3·75; N, 15·7; Cl, 13·3%).

Conversion of Nitro-3-aryl-(II; R' = H) *and Nitro-3-aryl-4-methyl-phthalaz-1-ones* (II; R' = Me) *into the Corresponding Phthalaz-4-ones* (IV; R' = H or Me).—The best conditions for effecting this conversion were determined and the influence of substituents in the 3-phenyl group was then examined. In general, the conversion was effected by heating (II; R' = H or Me) (1—1·5 g.) with dilute hydrochloric acid (18 c.c.; various strengths) in a sealed tube at 160—190° for a definite period (usually 6 hours). At the end of the reaction, the tube normally contained a mass of brownish-coloured crystals, sometimes slightly charred. After cooling and filtering, the crystals and filtrate were examined separately. The crystals consisted mainly of (IV), but sometimes contained some (II) or its hydrochloride, whereas the filtrate contained only unaltered (II). According to the particular compound (II) employed, the product was purified in one or several of three ways: (a) extraction with warm dilute hydrochloric acid, in which only compounds (II) are soluble, and this resulted in a good separation in many cases; (b) extraction with warm aqueous sodium hydroxide, in which only compounds (II) are soluble; or (c) extraction with boiling benzene, in which compounds (IV) are readily

soluble, whereas compounds (II) are almost insoluble. Separation can be effected almost quantitatively by these methods, and the yields of compounds (IV) given below are those obtained after complete removal of unaltered (II).

Conversion of (II; R = *4′-Nitrophenyl*, R′ = H) *into* (IV; R = *4′-Nitrophenyl*, R′ = H).—Compound (II) (1·5 g.) (J., 1928, 2553) was heated with (i) dilute hydrochloric acid (18 c.c.; 1 : 8), (ii) dilute sulphuric acid (18 c.c.; 1 : 8), (iii) water (18 c.c.), or (iv) aqueous sodium hydroxide (16 c.c.; 1 : 20), at 180° for 6 hours in each case. 4′-Nitro-3-phenylphthalaz-4-one was obtained from (i) and (ii) and crystallised from glacial acetic acid in fine, colourless, silky needles, m. p. and mixed m. p. with a synthetic specimen (*ibid.*, p. 2555) 258° [yield: (i) 1·00 g., 66·6%, (ii) 0·31 g., 20·6%]. There was no conversion in (iii) and decomposition occurred in (iv).

Conversion of (II; R = *4′-Nitrophenyl*, R′ = Me) *into* (IV; R = *4′-Nitrophenyl*, R′ = Me).—(a) *Variation in reagent.* Compound (II) (1·5 g.) (J., 1931, 1070) was heated with (i) dilute hydrochloric acid (18 c.c.; 1 : 8), (ii) dilute sulphuric acid (18 c.c.; 1 : 8), (iii) dilute acetic acid (18 c.c.; 1 : 8), or (iv) water (18 c.c.), at 180° for 6 hours in each case. 4′-Nitro-3-phenyl-1-methylphthalaz-4-one crystallised from glacial acetic acid in fine, colourless, silky needles, m. p. and mixed m. p. with a synthetic specimen (*ibid.*, p. 1924) 214° [yield: (i) 1·23 g., 82%; (ii) 1·10 g., 73·3%; (iii) 0·41 g., 27·3%; (iv) nil]. (b) *Variation in time.* Compound (II) (1 g.) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 180° for various times. In each case, both (IV) and unaltered (II) were isolated, and the velocity constant $1/t. \log 100/(100 - x)$ for a unimolecular reaction was calculated:

Time (minutes) (t)	90	125	182	270	360	540
% (IV) (x)	38	47	59	69	82	89
% (II) recovered	55	47	31	25	11	3
$k \times 10^4$	53	51	49	43	48	43

(c) *Variation in strength of acid.* Compound (II) (1 g.) was heated with dilute hydrochloric acid at 180° for 6 hours:

10N-Acid, c.c.	0·5	1	1·5	2	3	5	10	18
Water, c.c.	17·5	17	16·5	16	15	13	8	—
(IV), %	74	81	82	82	77	73	54	19
$k \times 10^4$	37	46	48	48	41	36	22	6

(d) *Variation in ratio of* (II) *to acid.* Compound (II) was heated with dilute hydrochloric acid (1 : 8) at 180° for 6 hours:

(II), g.	1	1	1	0·5	0·5
Acid, c.c.	10	18	25	18	25
(IV), %	81	82	81	80	78

(e) *Variation in temperature.* Compound (II) (1 g.) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 150° for 6 hours [yield of (IV), 0·23 g.; 23%]. The conversion was also effected by refluxing (II) (1 g.) with dilute hydrochloric acid [25 c.c.; (i) 1 : 5·25, (ii) 1 : 11·5] for 12 hours [yield: (i) 9%, (ii) 19%].

Conversion of (II; R = *4′-Nitro-2′-methylphenyl*, R′ = H) *into* (IV; R = *4′-Nitro-2′-methylphenyl*, R′ = H).—The preparation of (II) (J., 1932, 479) was improved. Compound (I; R = 4′-nitro-2′-methylphenyl) (10 g.) was refluxed with concentrated sulphuric acid (50 c.c.) and water (60 c.c.) for 1 hour; the solution was then diluted with water (110 c.c.), boiled (charcoal), and filtered hot. The sulphate crystallised on cooling and was neutralised. Compound (II) (1·5 g.) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 180° for 6 hours. 4′-Nitro-3-phenyl-2′-methylphthalaz-4-one crystallised from alcohol in colourless needles, m. p. and mixed m. p. with a synthetic specimen (*ibid.*, p. 482) 188° (yield, 0·30 g.; 20%).

Conversion of (II; R = *4′-Nitro-2′-methylphenyl*, R′ = Me) *into* (IV; R = *4′-Nitro-2′-methylphenyl*, R′ = Me).—Compound (II) (1·5 g.) (*ibid.*, p. 481) was best heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 160° for 6 hours, because much decomposition of (IV) occurred at 180°. 4′-Nitro-3-phenyl-1 : 2′-dimethylphthalaz-4-one crystallised from alcohol in almost colourless needles, m. p. and mixed m. p. with a synthetic specimen (J., 1936, 314) 178° (yield, 0·41 g.; 27·3%).

Conversion of (II; R = *2′-Chloro-4′-nitrophenyl*, R′ = Me) *into* (IV; R = *2′-Chloro-4′-nitrophenyl*, R′ = Me).—Compound (II) (1 g.) (J., 1932, 17) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 190° for 6 hours, because the use of a lower temperature resulted in the formation of (VI; R = 2′-chloro-4′-nitrophenyl) (see p. 103). 2′-Chloro-4′-nitro-3-phenyl-1-

methylphthalaz-4-one crystallised from alcohol in colourless prisms, m. p. and mixed m. p. with a synthetic specimen (J., 1936, 314) 206° (yield, 0·49 g.; 49%).

Conversion of (II; R = *2'-Bromo-4'-nitrophenyl*, R' = Me) *into* (IV; R = *2'-Bromo-4'-nitrophenyl*, R' = Me).—Compound (II) (1 g.) (J., 1935, 1137) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 200° for 6 hours, because the use of a lower temperature resulted in the formation of (VI; R = 2'-bromo-4'-nitrophenyl) (see p. 104). 2'-Bromo-4'-nitro-3-phenyl-1-methylphthalaz-4-one crystallised from alcohol in colourless needles, m. p. and mixed m. p. with a synthetic specimen (*loc. cit.*) 200—202° (yield, 0·27 g.; 27%).

Conversion of (II; R = 2' : *6'-Dichloro-4'-nitrophenyl*, R' = H) *into* (IV; R = 2' : *6'-Dichloro-4'-nitrophenyl*, R' = H).—Compound (II) (1·5 g.) (J., 1931, 1084) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at (i) 180°, or (ii) 170°, for 6 hours. 2' : 6'-Dichloro-4'-nitro-3-phenylphthalaz-4-one crystallised from alcohol in colourless needles, m. p. and mixed m. p. with a synthetic specimen (J., 1936, 313) 179° [yield: (i) 0·70 g., 46·6%; (ii) 0·51 g., 34%].

Conversion of (II; R = 2' : *6'-Dichloro-4'-nitrophenyl*, R' = Me) *into* (IV; R = 2' : *6'-Dichloro-4'-nitrophenyl*, R' = Me).—Compound (II) (1 g.) (J., 1931, 1085) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 200° for 6 hours, because the use of a lower temperature resulted in the formation of (VI; R = 2' : 6'-dichloro-4' nitrophenyl) (see p. 104) and a mixture was obtained even at 190°. 2' : 6'-Dichloro-4'-nitro-3-phenyl-1-methylphthalaz-4-one crystallised from alcohol in colourless needles, m. p. and mixed m. p. with a synthetic specimen (J., 1936, 315) 235° (yield, 0·17 g.; 17%).

Conversion of (II; R = 2' : *6'-Dibromo-4'-nitrophenyl*, R' = H) *into* (IV; R = 2' : *6'-Dibromo-4'-nitrophenyl*, R' = H).—Compound (II) (1·5 g.) (J., 1931, 1084) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 165° for 10 hours, because much decomposition occurred at higher temperatures, *e.g.*, 180°. 2' : 6'-Dibromo-4'-nitro-3-phenylphthalaz-4-one crystallised from alcohol in colourless needles, m. p. and mixed m. p. with a synthetic specimen (J., 1936, 313) 190° (yield, 0·30 g.; 20%).

Attempted Conversion of (II; R = 2' : *6'-Dibromo-4'-nitrophenyl*, R' = Me) *into* (IV; R = 2' : *6'-Dibromo-4'-nitrophenyl*, R' = Me).—Compound (II) (1·5 g.) (J., 1931, 1085) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at (i) 165°, (ii) 180°, or (iii) 200°, for 6 hours. In each case, the product melted from 219—225° and appeared to be a mixture of 2' : 6'-dibromo-4'-nitro-3-phenyl-1-methylphthalaz-4-one (J., 1936, 315) and (VI; R = 2' : 6'-dibromo-4'-nitrophenyl) (see p. 104), from which neither was isolated pure.

Conversion of (II; R = *3'-Nitrophenyl*, R' = H) *into* (IV; R = *3'-Nitrophenyl*, R' = H).—Compound (II) (1·5 g.) (J., 1928, 2561) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 180° for (i) 6 hours, or (ii) 40 hours. 3'-Nitro-3-phenylphthalaz-4-one crystallised from alcohol in almost colourless needles, m. p. and mixed m. p. with a synthetic specimen (*ibid.*, p. 2563) 240° [yield: (i) 0·21 g., 14%; (ii) 0·92 g., 61·3%].

Conversion of (II; R = *3'-Nitrophenyl*, R' = Me) *into* (IV; R = *3'-Nitrophenyl*, R' = Me).—Compound (II) (1 g.) (J., 1936, 1709) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 160° for 6 hours, because much decomposition of (IV) occurred at 180°. 3'-Nitro-3-phenyl-1-methylphthalaz-4-one crystallised from alcohol in colourless needles, m. p. and mixed m. p. with a synthetic specimen (J., 1931, 1925) 167° (yield, 0·25 g.; 25%).

Conversion of (II; R = *2'-Nitrophenyl*, R' = Me) *into* (IV; R = *2'-Nitrophenyl*, R' = Me).—In the preparation of (II) (J., 1935, 1807), instead of neutralising the reaction mixture with sodium carbonate, it is advantageous to filter the crystalline complex salt that separates and neutralise it with ammonia. Compound (II) (1·5 g.) was heated with dilute hydrochloric acid [18 c.c.; (i) 1 : 35, (ii) 1 : 17, or (iii) 1 : 8] at 180° for 6 hours, or (iv) (II) (1 g.) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 180° for 1 hour. 2'-Nitro-3-phenyl-1-methylphthalaz-4-one crystallised from alcohol in colourless prisms, m. p. and mixed m. p. with a synthetic specimen (J., 1931, 1924) 202° [yield: (i) 1·00 g., 66·6%); (ii) 1·06 g., 70·6%; (iii) 0·98 g., 65·3%; (iv) 0·49 g., 49%]. The use of a lower temperature than 180° resulted in the formation of (VI; R = 2'-nitrophenyl) (see p. 102).

Conversion of (II; R = *2'-Nitro-4'-methylphenyl*, R' = H) *into* (IV; R = *2'-Nitro-4'-methylphenyl*, R' = H).—Compound (II) (1·5 g.) (J., 1936, 1107) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 170° for 6 hours. 2'-Nitro-3-phenyl-4'-methylphthalaz-4-one crystallised from alcohol in colourless prisms, m. p. and mixed m. p. with a synthetic specimen (p. 97) 195° (yield, 0·54 g.; 36%).

Conversion of (II; R = *2'-Nitro-4'-methylphenyl*, R' = Me) *into* (IV; R = *2'-Nitro-4'-methylphenyl*, R' = Me).—Compound (II) (1 g.) (J., 1936, 1108; preferably isolated *via* the

complex salt as described above for the 2′-nitro-analogue) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 185° for 6 hours, because the use of a lower temperature resulted in formation of (VI; R = 2′-nitro-4′-methylphenyl) (see p. 102). 2′-Nitro-3-phenyl-1 : 4′-dimethylphthalaz-4-one crystallised from alcohol in colourless prisms, m. p. and mixed m. p. with a synthetic specimen (p. 98) 258° (yield, 0·53 g.; 53%).

Conversion of (II; R = *4′-Chloro-2′-nitrophenyl*, R′ = H) *into* (IV; R = *4′-Chloro-2′-nitrophenyl*, R′ = H).—Compound (II) (1·5 g.) (J., 1935, 1806) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 180° for 6 hours. 4′-Chloro-2′-nitro-3-phenylphthalaz-4-one crystallised from glacial acetic acid in colourless, prismatic needles, m. p. and mixed m. p. with a synthetic specimen (p. 97) 213—214° (yield, 1·02 g.; 68%).

Conversion of (II; R = *4′-Chloro-2′-nitrophenyl*, R′ = Me) *into* (IV; R = *4′-Chloro-2′-nitrophenyl*, R′ = Me).—Compound (II) (1·5 g.) (J., 1935, 1807; with modified method of isolation as for the 2′-nitro-analogue above) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 190° for 6 hours, because the use of a lower temperature resulted in the formation of (VI; R = 4′-chloro-2′-nitrophenyl) (see p. 103). 4′-Chloro-2′-nitro-3-phenyl-1-methylphthalaz-4-one crystallised from glacial acetic acid in colourless prisms, m. p. and mixed m. p. with a synthetic specimen (p. 98) 261° (yield, 1·11 g.; 74%).

Proof of the Intramolecular Character of the Conversion of (II; R = *Nitroaryl*, R′ = H or Me) *into* (IV; R = *Nitroaryl*, R′ = H or Me).—A mixture of (II; R = 2′ : 6′-dichloro-4′-nitrophenyl, R′ = H) (1 g.) and (II; R = 4′-nitrophenyl, R′ = Me) (1 g.) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 180° for 6 hours. The product, after removal of unaltered phthalaz-1-ones, crystallised from alcohol in almost colourless needles, m. p. 206—207° (X).

Mixed Melting Points of 2′ : 6′-*Dichloro*-4′-*nitro*-3-*phenylphthalaz*-4-*one* (*A*) *and* 4′-*Nitro*-3-*phenyl*-1-*methylphthalaz*-4-*one* (*B*).

A, % by wt. ...	0	5	13	26	30	40	46	51	68	89	100
M. p.	214°	208°	202°	192°	188°	169°	162°	163°	168°	174°	179°

The product (X) corresponded in all respects with a mixture (Y) prepared from 8% of (A) and 92% of (B); the mixture (Y) melted at 206—207°, as did also a mixture of (X) and (Y). Pure (A) (0·008 g.) was then added to (X) (0·013 g.) to give a mixture which should consist of 44% of (A) and 56% of (B); this mixture melted at 166°, which corresponded with the m. p. of a mixture of 43% of (A) and 57% of (B). It was concluded, therefore, that the original mixture (X) consisted solely of (A) and (B) in the proportion 8 : 92. The great difference between the quantities of (A) and (B) formed in the conversion is due to the greater reaction velocity in the case of (II; R = 4′-nitrophenyl, R′ = Me) than in the case of (II; R = 2′ : 6′-dichloro-4′-nitrophenyl, R′ = H).

Conversion of Certain Nitro-3-*aryl*-4-*methylphthalaz*-1-*ones* (II; R′ = Me) *into* 2-(*Nitroarylamino*)-3-*methylene*isoindolinones (VI; R = nitroaryl).—In general, this conversion was effected by heating (II; R′ = Me) (1—1·5 g.) with dilute hydrochloric acid (18 c.c.; various strengths) in a sealed tube at a temperature lower than that required for conversion into (IV; R′ = Me). Conversion was readily effected by refluxing (II; R = 2′-nitroaryl, R′ = Me) with dilute hydrochloric acid, but with such 4′-nitro-analogues as undergo the conversion, temperatures of 150—170° were necessary. Unaltered (II) was removed from the product by extraction with boiling dilute hydrochloric acid (1 : 1); separation was also possible by means of the greater solubility of (VI) in boiling benzene.

Reactions of 2-(*Nitroarylamino*)-3-*methylene*isoindolinones.—*Hydrolysis*. Compound (VI) (1 g.) was refluxed with alcoholic sodium ethoxide (0·2 g. of sodium in 25 c.c. of alcohol) until the colour of the solution changed from bright red to reddish-brown (20—45 minutes). The mixture was poured on ice (50 g.) and acidified with hydrochloric acid, and the *o*-carboxyacetophenonenitroarylhydrazone (III; R′ = Me) collected. *Reduction*. (a) Compound (VI) (1 g.) was refluxed with a solution of sodium sulphide crystals (10 g.) in water (50 c.c.) and alcohol (50 c.c.) until almost colourless crystals of the amino-3-aryl-1-methylphthalaz-4-one (IV; R′ = Me) separated from the orange solution (30—45 minutes). (b) Iron powder (0·75 g.) was added to a boiling solution of (VI) (1 g.) in glacial acetic acid (25 c.c.) and water (10 c.c.). The resulting green solution was diluted with water (50 c.c.) and partly neutralised with aqueous sodium hydroxide until brownish crystals of the 2-(aminoarylamino)-3-methylene*iso*indolinone (VI; R = aminoaryl) separated. *Oxidation*. A solution of chromium trioxide (0·5 g.) in water (10 c.c.) was added to a solution of (VI) (1 g.) in glacial acetic acid (25 c.c.) at 80°, and the *N*-nitroarylaminophthalimide precipitated by dilution with water (100 c.c.). *Action of mineral*

acids. (a) Compound (VI) (1·5 g.) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) in a sealed tube at 180—200° for 6 hours. (b) A solution of (VI) (1 g.) in concentrated sulphuric acid (25 c.c.) was heated at 180° for a few minutes until the deep reddish-brown colour had changed to pale yellow. After cooling, the nitro-3-aryl-1-methylphthalaz-4-one (IV; R' = Me) was precipitated by pouring the solution on ice (100 g.).

Conversion of (II; R = 2'-Nitrophenyl, R' = Me) into (VI; R = 2'-Nitrophenyl).—(a) Compound (II) (2 g.) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 160° for 6 hours (yield, 1·51 g.; 75·5%). *Variation in strength of acid.* Compound (II) (1·5 g.) was heated with water, or dilute hydrochloric acid, at 150° for 6 hours:

10*N*-Acid, c.c.	—	0·11	0·22	0·5	0·78	1	2	4	9	18
Water, c.c.	18	17·89	17·78	17·5	17·12	17	16	14	9	—
(VI), g.	0·37	1·32	1·37	1·26	1·23	1·14	0·98	0·55	0·05	—
(VI), %	24·6	88	91·3	84	82	76	65·3	36·6	3·3	—

(b) Compound (II) (5 g.) was refluxed with dilute hydrochloric acid (125 c.c.; 1 : 11·5) for 1½ hours (yield, 4·8 g.; 96%). *Variations in strength of acid and time.* Compound (II) (1 g.) was refluxed with dilute hydrochloric acid [25 c.c.; (i) 1 : 4, (ii) 1 : 11·5, (iii) 1 : 24].

(i) No conversion occurred after ½ hour.

(ii)

Time (minutes) (t)	5	7	10	12	15	17	20	30
(VI) (x), %	19	23	32	41	48	53	58	66
$k \times 10^3$	42	37	38	44	43	45	43	36

(iii) The yield of (VI) was 10% after 5 minutes and 20% after 10 minutes.

2-(2'-*Nitrophenylamino*)-3-*methylene*iso*indolinone* crystallised from alcohol or glacial acetic acid in yellow prismatic needles and from benzene in yellow hexagonal plates, m. p. 179° (Found: C, 64·2; H, 4·0; N, 15·0. $C_{15}H_{11}O_3N_3$ requires C, 64·05; H, 3·9; N, 14·95%), soluble in boiling aqueous-alcoholic sodium hydroxide with a deep crimson colour and insoluble in hydrochloric acid. *Hydrolysis.* *o*-Carboxyacetophenone-2'-nitrophenylhydrazone crystallised from alcohol in orange prisms, m. p. and mixed m. p. with a synthetic specimen (J., 1931, 1924) 184° (yield, 0·95 g.; 89·3%), converted by cold concentrated sulphuric acid into 2'-nitro-3-phenyl-1-methylphthalaz-4-one, m. p. 202°. *Reduction.* (a) 2'-Amino-3-phenyl-1-methylphthalaz-4-one crystallised from alcohol in colourless needles, m. p. and mixed m. p. with a synthetic specimen (p. 97) 241° (yield, 0·6 g.; 67·2%). (b) 2-(2'-*Aminophenylamino*)-3-*methylene*iso*indolinone* crystallised from alcohol in colourless rectangular plates, m. p. 227—228° (decomp.) after becoming brown at 220° (yield, 0·52 g.; 58·2%) (Found: C, 72·1; H, 5·35; N, 17·25. $C_{15}H_{13}ON_3$ requires C, 71·7; H, 5·2; N, 16·7%). When (0·5 g.) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) in a sealed tube at 180° for 6 hours, and the mixture rendered alkaline with sodium hydroxide, 2' : 4-anhydro-2'-amino-3-phenyl-1-methylphthalaz-4-one, colourless feathery needles, m. p. and mixed m. p. with the specimen already described (p. 98) 163° (yield, 0·41 g.; 88·3%), was obtained. *Oxidation.* *N*-2'-Nitrophenylaminophthalimide (phthalyl-2'-nitrophenylhydrazide) crystallised from glacial acetic acid in pale yellow prisms, m. p. and mixed m. p. with a synthetic specimen (J., 1935, 1812) 293—294° (yield, 0·65 g.; 64·5%). *Action of mineral acids.* 2'-Nitro-3-phenyl-1-methylphthalaz-4-one crystallised from alcohol in colourless prisms, m. p. and mixed m. p. with a synthetic specimen 202° [yield: (a) 1·10 g., 73·3%; (b) 0·96 g., 96%].

Conversion of (II; R = 2'-Nitro-4'-methylphenyl, R' = Me), into (VI; R = 2'-Nitro-4'-methylphenyl).—(a) Compound (II) (1·5 g.) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 160° for 6 hours (yield, 0·66 g.; 44%). *Variation in strength of acid.* Compound (II) (1 g.) was heated with water, or dilute hydrochloric acid, at 160° for 6 hours:

10*N*-Acid, c.c.	—	0·22	0·5	1	2
Water, c.c.	18	17·78	17·5	17	16
(VI), %	33	88	81	67	44

(b) Compound (II) (5 g.) was refluxed with dilute hydrochloric acid (125 c.c.; 1 : 24) for 1½ hours (yield, 4·65 g.; 93%). *Variation in time.* Compound (II) (1 g.) was refluxed with dilute hydrochloric acid (25 c.c.; 1 : 11·5):

Time (minutes)	10	15	20	30
(VI), %	14	23	27	38

2-(2'-*Nitro-4'-methylphenylamino*)-3-*methylene*iso*indolinone* crystallised from alcohol in bright yellow needles, m. p. 194° (Found: C, 65·15; H, 4·55; N, 14·2. $C_{16}H_{13}O_3N_3$ requires C, 65·1; H, 4·4; N, 14·2%), soluble in boiling aqueous-alcoholic sodium hydroxide with a

bluish-red colour. *Hydrolysis.* o-Carboxyacetophenone-2'-nitro-4'-methylphenylhydrazone crystallised from alcohol in orange feathery needles, m. p. and mixed m. p. with a synthetic specimen (p. 98) 175°, resolidifying and melting again at 256—257° (yield, 0·92 g.; 86·7%). *Reduction.* (a) 2'-Amino-3-phenyl-1 : 4'-dimethylphthalaz-4-one crystallised from alcohol in colourless needles, m. p. and mixed m. p. with a synthetic specimen (p. 98) 203° (yield, 0·67 g.; 74·6%). (b) Although a variety of conditions were used, little product could be isolated. This crystallised from dilute alcohol in brownish plates, m. p. 237° (decomp.) with previous darkening, and was probably 2-(2'-amino-4'-methylphenylamino)-3-methylene*iso*indolinone, but the quantity was insufficient for analysis. *Oxidation.* N-2'-Nitro-4'-methylphenylaminophthalimide crystallised from glacial acetic acid in yellow prismatic needles, m. p. and mixed m. p. with a synthetic specimen (see below) 263° (yield, 0·58 g.; 57·6%). *Action of mineral acids.* 2'-Nitro-3-phenyl-1 : 4'-dimethylphthalaz-4-one crystallised from alcohol in colourless prisms, m. p. and mixed m. p. with a synthetic specimen 258° [yield: (a) 0·87 g., 58%; (b) 0·92 g., 92%].

o-Carboxybenzo-2'-nitro-4'-methylphenylhydrazide.—Solutions of o-nitro-p-tolylhydrazine (2 g. in 200 c.c.) and of phthalic anhydride (2 g. in 50 c.c.) in chloroform were mixed and the yellow needles formed were filtered off after 12 hours. o-*Carboxybenzo-2'-nitro-4'-methylphenylhydrazide* crystallised from chloroform in yellow needles, m. p. 260—261° (yield, 3·5 g.; 92·8%) (Found: N, 13·25. $C_{15}H_{13}O_5N_3$ requires N, 13·3%), soluble in cold dilute sodium carbonate solution with an intense violet colour.

N-2'-*Nitro-4'-methylphenylaminophthalimide*, produced when the above o-carboxy-hydrazide (2 g.) was dissolved in boiling glacial acetic acid, crystallised from this solvent in yellow prismatic needles, m. p. 263° (yield, 1·7 g.; 90·1%) (Found: C, 60·3; H, 3·9; N, 14·35. $C_{15}H_{11}O_4N_3$ requires C, 60·6; H, 3·7; N, 14·15%), soluble in boiling dilute sodium hydroxide solution with a violet colour owing to regeneration of the o-carboxy-hydrazide.

Conversion of (II; R = 4'-*Chloro-2'-nitrophenyl*, R' = Me) *into* (VI; R = 4'-*Chloro-2'-nitrophenyl*).—(a) Compound (II) (1·5 g.) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 160° for 6 hours (yield, 1·08 g.; 72%). (b) Compound (II) (5 g.) was refluxed with dilute hydrochloric acid (125 c.c.; 1 : 24) for 1 hour (yield, 4·8 g.; 96%). *Variation in strength of acid.* Compound (II) (1 g.) was refluxed with dilute hydrochloric acid [25 c.c.; (i) 1 : 11·5, (ii) 1 : 24] for ½ hour [yield: (i) 78%, (ii) 91%].

2-(4'-*Chloro-2'-nitrophenylamino*)-3-*methylene*iso*indolinone* crystallised from alcohol in yellow needles, m. p. 224° (Found: C, 56·75; H, 3·35; N, 13·4; Cl, 10·95. $C_{15}H_{10}O_3N_3Cl$ requires C, 57·05; H, 3·15; N, 13·3; Cl, 11·25%), soluble in boiling aqueous-alcoholic sodium hydroxide with an intense bluish-red colour. *Hydrolysis.* o-Carboxyacetophenone-4'-chloro-2'-nitrophenylhydrazone crystallised from alcohol in orange feathery needles, m. p. and mixed m. p. with a synthetic specimen (p. 98) 185—186° (yield, 0·88 g.; 83·3%). *Reduction.* (a) 4'-Chloro-2'-amino-3-phenyl-1-methylphthalaz-4-one crystallised from alcohol in colourless needles, m. p. and mixed m. p. with a synthetic specimen (p. 98) 222—223° (yield, 0·62 g.; 68·5%). (b) 2-(4'-*Chloro-2'-aminophenylamino*)-3-*methylene*iso*indolinone* crystallised from alcohol in colourless rectangular plates, m. p. 228° (decomp.) after darkening at 210° (yield, 0·55 g.; 60·8%) (Found: C, 63·1; H, 4·25; N, 14·45. $C_{15}H_{12}ON_3Cl$ requires C, 63·05; H, 4·2; N, 14·7%). *Oxidation.* N-4'-Chloro-2'-nitrophenylaminophthalimide crystallised from glacial acetic acid in yellow needles, m. p. and mixed m. p. with a synthetic specimen (see below) 265° (yield, 0·56 g.; 55·6%). *Action of mineral acids.* 4'-Chloro-2'-nitro-3-phenyl-1-methylphthalaz-4-one crystallised from alcohol in colourless prisms, m. p. and mixed m. p. with a synthetic specimen 261° [yield: (a) 0·94 g., 62·6%; (b) 0·96 g., 96%].

N-4'-*Chloro-2'-nitrophenylaminophthalimide*, prepared similarly to the 2'-nitro-4'-methyl-analogue (above), *via* o-*carboxybenzo-4'-chloro-2'-nitrophenylhydrazide*, yellow prismatic needles, m. p. 263—264° (yield, 95%) (Found: N, 12·75; Cl, 10·8. $C_{14}H_{10}O_5N_3Cl$ requires N, 12·5; Cl, 10·6%), crystallised from glacial acetic acid in yellow needles, m. p. 265° (yield, 90%) (Found: C, 52·9; H, 2·6; N, 13·35; Cl, 11·05. $C_{14}H_8O_4N_3Cl$ requires C, 52·9; H, 2·5; N, 13·2; Cl, 11·2%), soluble in boiling dilute sodium hydroxide solution with an intense violet colour owing to regeneration of the o-carboxy-hydrazide.

Conversion of (II; R = 2'-*Chloro-4'-nitrophenyl*, R' = Me) *into* (VI; R = 2'-*Chloro-4'-nitrophenyl*).—Compound (II) (1 g.) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) in a sealed tube at 160° for 6 hours. 2-(2'-*Chloro-4'-nitrophenylamino*)-3-*methylene*iso*indolinone* crystallised from alcohol in pale yellow prisms, m. p. 164° (yield, 0·66 g.; 66%) (Found: C, 56·9; H, 3·35; N, 13·7; Cl, 10·8. $C_{15}H_{10}O_3N_3Cl$ requires C, 57·05; H, 3·15; N, 13·3; Cl, 11·25%), soluble in boiling aqueous-alcoholic sodium hydroxide with a deep red colour. *Hydrolysis.* o-Carboxyacetophenone-2'-chloro-4'-nitrophenylhydrazone crystallised from alcohol

in orange-yellow needles, m. p. and mixed m. p. with a synthetic specimen (J., 1936, 314) 160° (yield, 0·92 g.; 87%). *Reduction.* (a) 2'-Chloro-4'-amino-3-phenyl-1-methylphthalaz-4-one crystallised from alcohol in colourless prisms, m. p. and mixed m. p. with a synthetic specimen (*loc. cit.*) 197° (yield, 0·56 g.; 61·9%). *Action of mineral acid.* Method (b), but at 200°. 2'-Chloro-4'-nitro-3-phenyl-1-methylphthalaz-4-one crystallised from alcohol in colourless prisms, m. p. and mixed m. p. with a synthetic specimen 206° (yield, 0·9 g.; 90%).

Conversion of (II; R = 2'-*Bromo-4'-nitrophenyl*, R' = Me) *into* (VI; R = 2'-*Bromo-4'-nitrophenyl*).—Compound (II) (1 g.) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 165° for 6 hours (the yield was halved at 160°). 2-(2'-*Bromo-4'-nitrophenylamino*)-3-*methylene*-iso*indolinone* crystallised from alcohol in pale brownish-yellow, prismatic needles, m. p. 201° (yield, 0·65 g.; 65%) (Found: C, 50·2; H, 3·15; N, 11·4; Br, 22·35. $C_{15}H_{10}O_3N_3Br$ requires C, 50·0; H, 2·8; N, 11·65; Br, 22·2%), soluble in boiling aqueous-alcoholic sodium hydroxide with an intense red colour. *Hydrolysis.* *o*-Carboxyacetophenone-2'-bromo-4'-nitrophenylhydrazone crystallised from alcohol in orange-yellow needles, m. p. and mixed m. p. with a synthetic specimen (J., 1935, 1137) 154° (yield, 0·9 g.; 85·7%). *Reduction.* (a) 2'-Chloro-4'-amino-3-phenyl-1-methylphthalaz-4-one crystallised from alcohol in colourless needles, m. p. and mixed m. p. with a synthetic specimen (J., 1936, 315) 130° (decomp.) (yield, 0·56 g.; 61·1%). *Action of mineral acid.* Method (b), but at 200°. 2'-Bromo-4'-nitro-3-phenyl-1-methylphthalaz-4-one crystallised from alcohol in colourless prisms, m. p. and mixed m. p. with a synthetic specimen 200—202° (yield, 0·88 g.; 88%).

Conversion of (II; R = 2' : 6'-*Dichloro-4'-nitrophenyl*, R' = Me) *into* (VI; R = 2' : 6'-*Dichloro-4'-nitrophenyl*).—Compound (II) (1 g.) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 160° for 6 hours. 2-(2' : 6'-*Dichloro-4'-nitrophenylamino*)-3-*methylene*iso*indolinone* crystallised from alcohol in pale brownish-yellow, prismatic needles, m. p. 173° (yield, 0·36 g.; 36%) (Found: C, 51·6; H, 2·7; N, 12·0; Cl, 20·5. $C_{15}H_9O_3N_3Cl_2$ requires C, 51·4; H, 2·55; N, 12·0; Cl, 20·3%), soluble in boiling aqueous-alcoholic sodium hydroxide with a deep red colour. *Action of mineral acid.* Method (b), but at 200°. 2' : 6'-Dichloro-4'-nitro-3-phenyl-1-methylphthalaz-4-one crystallised from alcohol in colourless needles, m. p. and mixed m. p. with a synthetic specimen 235°.

Attempted Conversion of (II; R = 2' : 6'-*Dibromo-4'-nitrophenyl*, R' = Me) *into* (VI; R = 2' : 6'-*Dibromo-4'-nitrophenyl*) (cf. p. 100).—Compound (II) (1 g.) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) at 165° for 6 hours. The product, m. p. 219—221°, appeared to be a mixture of (VI; R = 2' : 6'-dibromo-4'-nitrophenyl) and 2' : 6'-dibromo-4'-nitro-3-phenyl-1-methylphthalaz-4-one, from which the former could not be isolated. This was confirmed by heating a solution of the mixture in concentrated sulphuric acid for a few minutes, only 2' : 6'-dibromo-4'-nitro-3-phenyl-1-methylphthalaz-4-one, m. p. and mixed m. p. with a synthetic specimen 237°, being obtained.

*Conversion of 2'-Amino-3-aryl-4-methylphthalaz-*1-*ones* (II; R' = Me) *and of 2'-Amino-3-arylphthalaz-*1-*one-4-acetic Acid Lactams* (VII) *into* 2' : 4-*Anhydro-2'-amino-3-aryl-*1-*methylphthalaz-4-ones* (V; R' = Me).—This conversion was effected by heating (a) (II; R = 2'-aminoaryl, R' = Me) (1 g.), and (b) (VII) (1 g.), with dilute hydrochloric acid (18 c.c.; 1 : 8) in a sealed tube at 180° for 6 hours. The resulting dark brown solution with a faint green fluorescence was rendered alkaline with aqueous sodium hydroxide; the brownish precipitate was collected, dried, and extracted with boiling benzene, and, after removal of the solvent from the extract, the residue (V; R' = Me) was crystallised repeatedly. When (II; R = 4'- or 3'-aminophenyl, R' = H or Me) was heated with dilute hydrochloric acid under the same conditions, no reaction occurred and in each case unaltered (II) was recovered almost quantitatively.

2' : 4-Anhydro-2'-amino-3-phenyl-1-methylphthalaz-4-one crystallised from methyl alcohol in colourless needles, m. p. and mixed m. p. with the specimen already described (p. 98) 163° [yield: (a) 0·47 g., 50·6%; (b) 0·40 g., 47·5%].

2' : 4-Anhydro-2'-amino-3-phenyl-1 : 4'-dimethylphthalaz-4-one crystallised from aqueous alcohol in pale cream-coloured needles, m. p. and mixed m. p. with the specimen already described (p. 98) 186° [yield: (b) 0·43 g., 50·7%]. In this case, the substance, colourless needles, m. p. 311—313° (decomp.) (J., 1936, 1107), was used, although repeated analyses of numerous samples did not support the constitution of 2'-amino-3-phenyl-4'-methylphthalaz-1-one-4-acetic acid lactam.

2' : 4-Anhydro-4'-chloro-2'-amino-3-phenyl-1-methylphthalaz-4-one crystallised from dilute acetic acid in long colourless needles, m. p. and mixed m. p. with the specimen already described (p. 98) 193° [yield: (a) 0·70 g., 74·7%; (b) 0·64 g., 74·5%].

Conversion of 2′-Amino-3-arylphthalaz-1-ones (II; R′ = H) *into a Mixture of* (VIII) *and* (IX).—This conversion was effected by heating (II; R = 2′-aminoaryl) (1·5 g.) with dilute hydrochloric acid (18 c.c.; 1 : 8) in a sealed tube at 180° for 6 hours. The resulting brown solution, containing pale brown crystals, was rendered alkaline with warm aqueous sodium hydroxide (evolution of ammonia) and filtered. The precipitate was dried and extracted with boiling benzene, the solvent removed from the extract, and the residue (IX) crystallised. The alkaline filtrate was acidified carefully with acetic acid, and the colourless precipitate (VIII) crystallised.

In the case of (II; R = 2′-aminophenyl, R′ = H), the sulphate (1·5 g.) (J., 1935, 1805) of the substance, which possessed the properties of 2′-amino-3-phenylphthalaz-1-one, although analyses did not support that constitution, was used. *o*-Benzylenebenziminazole crystallised from aqueous alcohol in colourless rectangular plates, m. p. and mixed m. p. with an authentic specimen (*ibid.*, p. 1806) 212° (yield, 0·06 g.; 6·8%), and 2-phenylbenziminazole-*o*-carboxylic acid crystallised from aqueous acetic acid in colourless needles, m. p. and mixed m. p. with an authentic specimen (*loc. cit.*) 270° (yield, 0·72 g.; 70·8%).

(II; R = 4′-Chloro-2′-aminophenyl, R′ = H) also was used. 5-Chloro-*o*-benzylenebenziminazole crystallised from aqueous alcohol in small colourless plates, m. p. and mixed m. p. with an authentic specimen (*loc. cit.*) 242° (yield, 0·20 g.; 15%), and 5-chloro-2-phenylbenziminazole-*o*-carboxylic acid crystallised from glacial acetic acid in small colourless needles, m. p. and mixed m. p. with an authentic specimen (*loc. cit.*) 285° (yield, 0·91 g.; 60·4%); (II) (0·15 g.; 10%) was recovered unaltered.

Action of Dilute Hydrochloric Acid on (I; R = 4′-*Nitrophenyl*).—Compound (I) (1·5 g.) was heated in a sealed tube with (a) dilute hydrochloric acid (18 c.c.; 1 : 2) at 150° for 12 hours, and (b) dilute hydrochloric acid (18 c.c.; 1 : 7·5) at 170—175° for 6 hours. After neutralisation with sodium carbonate, the sole reaction product isolated from (a) was 4′-nitro-3-phenylphthalaz-1-one, yellow needles, m. p. 333°. The product from (b), however, was a dark brown, semi-crystalline, slightly charred mass, which was collected, ground with cold sodium carbonate solution, washed with water, and dried (yield, 1 g.); it crystallised from alcohol–pyridine (6 : 1, charcoal) in straw-coloured needles, m. p. 217—219° (X) (Found: C, 63·65; H, 3·65; N, 14·9. Calc. for $C_{14}H_9O_3N_3$: C, 62·9; H, 3·4; N, 15·7. Calc. for $C_{15}H_{11}O_3N_3$: C, 64·05; H, 3·9; N, 14·95%) (cf. J., 1933, 1068). Repeated crystallisations from this mixture of solvents gave pale straw-coloured, silky needles, m. p. 221—222° (Found: C, 63·7; H, 3·7; N, 15·3%), two further crystallisations from glacial acetic acid gave almost colourless, silky needles, m. p. 226—227° (Found: C, 63·4; H, 3·7; N, 15·3%), and a final crystallisation from nitrobenzene gave long, colourless, silky needles, m. p. 228—230° (Found: C, 63·35; H, 3·7; N, 15·4%). In all cases, melting was preceded by softening, and the products possessed all the properties of mixtures of 4′-nitro-3-phenyl- and 4′-nitro-3-phenyl-1-methyl-phthalaz-4-one, from which neither could be isolated by fractional crystallisation. This was supported by examination of deliberately prepared mixtures of the two compounds, as well as by the above analytical results.

Mixed Melting Points of 4′-Nitro-3-phenylphthalaz-4-one (A) and 4′-Nitro-3-phenyl-1-methyl-phthalaz-4-one (B).

(A), % by wt.	0	33	40	50	60	72	100
M. p.	214°	209°	211°	215°	226°	237°	258°
M. p. after one crystn. from glacial acetic acid	—	213°	218°	225°	233°	240°	—

A mixture, which corresponded in all respects with (X), was prepared by dissolving (A) (0·4 g.) and (B) (0·6 g.) in boiling glacial acetic acid and collecting the colourless needles (Y) after 15 minutes when the temperature had fallen to 55°; the mixture (Y) [Found: C, 63·65; H, 3·85; N, 15·3. Calc. for a mixture of 45% of (A) and 55% of (B): C, 63·55; H, 3·7; N, 15·3%], (X), and a mixture of (X) and (Y), all melted at 217—219°.

When (X) (2 g.) was reduced by boiling with a solution of sodium sulphide crystals (6 g.) in water (20 c.c.) and alcohol (10 c.c.) for 20 minutes, brownish prisms (1·1 g.), m. p. 184—187°, separated on cooling. Prolonged fractional crystallisation from alcohol gave a little 4′-amino-3-phenyl-1-methylphthalaz-4-one, almost colourless prisms, m. p. 201—203° (Found: C, 71·35; H, 5·2; N, 16·85. Calc. for $C_{15}H_{13}ON_3$: C, 71·7; H, 5·2; N, 16·7%), and mixed m. p. with a synthetic specimen (J., 1935, 314) 203—204°; the acetyl derivative crystallised from alcohol in colourless needles, m. p. and mixed m. p. with an authentic specimen (*loc. cit.*) 252° (Found: C, 69·3; H, 5·0; N, 14·0. Calc. for $C_{17}H_{15}O_2N_3$: C, 69·6; H, 5·1; N, 14·3%).

Action of Dilute Hydrochloric Acid on (I; R = 3′-*Nitrophenyl*).—Compound (I) (2 g.) was

heated in a sealed tube with (a) dilute hydrochloric acid (18 c.c.; 1 : 7·5) at 170—175° for 6 hours, and (b) dilute hydrochloric acid (18 c.c.; 1 : 8) at 165° for 48 hours. The sole reaction product isolated from (a) was 3′-nitro-3-phenylphthalaz-1-one, pale yellow needles, m. p. 324°. The product from (b) was a mixture, which was separated in the usual manner into 3′-nitro-3-phenylphthalaz-4-one, colourless needles, m. p. and mixed m. p. 240° (yield, 0·6 g.; 36·8%), and 3′-nitro-3-phenylphthalaz-1-one, m. p. and mixed m. p. 324° (yield, 0·4 g.; 24·5%).

Action of Dilute Hydrochloric Acid on (I; R = *2′-Nitrophenyl*).—Compound (I) (1·5 g.) was heated in a sealed tube with dilute hydrochloric acid (18 c.c.; 1 : 8) at (a) 165°, (b) 175—180°, and (c) 190—195°, for 6 hours. No reaction occurred in (a) and (b), but in (c) a brown, slightly charred mass was obtained. The united product from four experiments was ground with sodium carbonate solution, then with sodium hydroxide solution, and washed with water, and the residue dried (yield, 1·8 g.). Repeated fractional crystallisation from alcohol (charcoal) gave colourless prisms, m. p. 176° after softening at 172° (X) [Found: C, 63·5; H, 3·95; N, 15·65. Calc. for a mixture of 50% of (A) and 50% of (B): C, 63·5; H, 3·65; N, 15·35%], and colourless prisms, m. p. 187° after softening at 182° (X′) [Found: C, 63·6; H, 3·75; N, 14·7. Calc. for a mixture of 25% of (A) and 75% of (B): C, 63·8; H, 3·8; N, 15·1%]. Both (X) and (X′) possessed all the properties of mixtures of 2′-nitro-3-phenyl- and 2′-nitro-3-phenyl-1-methyl-phthalaz-4-one, from which neither could be isolated by fractional crystallisation.

Mixed Melting Points of 2′-Nitro-3-phenylphthalaz-4-one (A) and 2′-Nitro-3-phenyl-1-methylphthalaz-4-one (B).

(A), % by wt. ...	0	22	32	39	46	50	55	69	75	88	100
M. p.	202°	189°	184°	179—180°	176°	176°	179°	185—186°	191°	196°	201°

The product (X) corresponded in all respects with a mixture (Y) prepared from 50% of (A) and 50% of (B); the mixture (Y) melted at 176°, as did also a mixture of (X) and (Y), and a mixture of (X) and (B), whereas a mixture of (X) and (A) melted at 182°. The product (X′) corresponded in all respects with a mixture (Y′) prepared from 25% of (A) and 75% of (B); the mixture (Y′) melted at 187°, as did also a mixture of (X′) and (Y′), whilst a mixture of (X′) and (A) melted at 181°, and a mixture of (X′) and (B) melted at 192—193°.

Action of Dilute Hydrochloric Acid on (I; R = *4′-Aminophenyl*).—Compound (I) (1·5 g.) was heated in a sealed tube with (a) dilute hydrochloric acid (18 c.c.; 1 : 2) at 150° for 12 hours, and (b) dilute hydrochloric acid (18 c.c.; 1 : 7·5) at 175° for 6 hours. In each case, the sole reaction product isolated was 4′-amino-3-phenylphthalaz-1-one, deep straw-coloured prisms, m. p. 259° (cf. J., 1933, 1068).

Action of Dilute Hydrochloric Acid on (I; R = *2′-Aminophenyl*).—Compound (I) (1·5 g.) was heated with dilute hydrochloric acid (18 c.c.; 1 : 8) in a sealed tube at 180° for 6 hours. The reaction mixture was rendered alkaline with warm aqueous sodium hydroxide (evolution of ammonia) and filtered. The precipitate was dried and extracted with boiling benzene, and the solvent removed from the extract; the residue of 2′ : 4-anhydro-2′-amino-3-phenyl-1-methylphthalaz-4-one crystallised from aqueous alcohol in colourless feathery needles, m. p. and mixed m. p. with the specimen already described (p. 98) 163° (yield, 0·43 g.; 37·4%). Careful acidification of the alkaline filtrate with acetic acid, followed by crystallisation of the precipitate from dilute acetic acid, gave 2-phenylbenziminazole-*o*-carboxylic acid, colourless needles, m. p. and mixed m. p. with an authentic specimen 270° (yield, 0·62 g.; 51·6%).

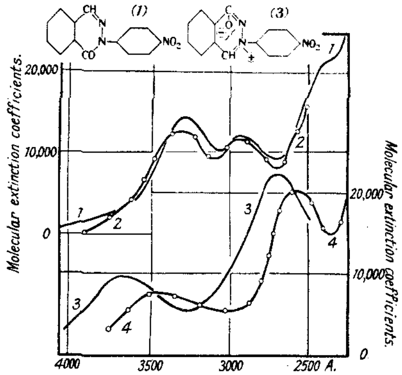
The Absorption Spectra of Certain Nitroarylphthalazones and Related Compounds (by A. E. GILLAM).

In view of the relationships that have now been established between the corresponding isomerides (II; R = nitroaryl, R′ = H) and (IV; R = nitroaryl, R′ = H) and between the corresponding isomerides (II; R = nitroaryl, R′ = Me), (IV; R = nitroaryl, R′ = Me), and (VI; R = nitroaryl), a study of the absorption spectra of some typical examples of these compounds appeared to be of interest. The apparatus used was a Hilger E_3 quartz spectrograph fitted with a Spekker photometer, a tungsten-steel high-tension spark being employed as the source of light. The solvent was in all cases ethyl alcohol specially purified until transparent down to about 2100 A.

The first group of compounds examined comprised 4′-nitro-3-phenylphthalaz-1-one (II; R = 4′-nitrophenyl, R′ = H), the corresponding 4-methyl compound (II; R′ = Me), 4′-nitro-3-phenylphthalaz-4-one (IV; R = 4′-nitrophenyl, R′ = H), and the corresponding 1-methyl compound (IV; R′ = Me). The absorption curves are reproduced in Fig. 3. It will be seen that (a) the absorption of the 1-ones is quite different from that of the 4-ones, and (b) the introduction of the 1-methyl group into the 4-one produces no appreciable change in

the absorption, whereas introduction of the 4-methyl group into the 1-one causes a displacement of the maxima towards the ultra-violet (3670 A. ⟶ 3460 A.).

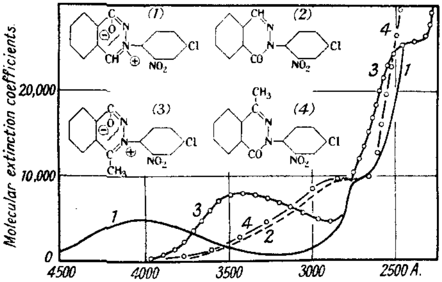
FIG. 3.



1. ———— 4′-*Nitro-3-phenylphthalaz-4-one.*
2. O——O 4′-*Nitro-3-phenyl-*1-*methylphthalaz-*4-*one.*
3. ———— 4′-*Nitro-3-phenylphthalaz-*1-*one.*
4. O——O 4′-*Nitro-3-phenyl-4-methylphthalaz-*1-*one.*

The methyl group is usually regarded as a transparent group, *i.e.*, one without chromophoric properties, but when a hydrogen atom is replaced by it the effect on the resulting absorption spectrum depends upon the position of the hydrogen atom relative to the chromophoric group.

FIG. 4.



1. ———— 4′-*Chloro-2′-nitro-3-phenylphthalaz-*1-*one.*
2. — — — 4′-*Chloro-2′-nitro-3-phenylphthalaz-4-one.*
3. O——O 4′-*Chloro-2′-nitro-3-phenyl-4-methylphthalaz-*1-*one.*
4. O- - -O 4′-*Chloro-2′-nitro-3-phenyl-*1-*methylphthalaz-4-one.*

In general, when a hydrogen atom not directly attached to a chromophoric group is replaced by methyl, the absorption spectrum is unaltered or only slightly altered, but when a hydrogen atom directly attached to an active chromophoric group is replaced by methyl, some displace-

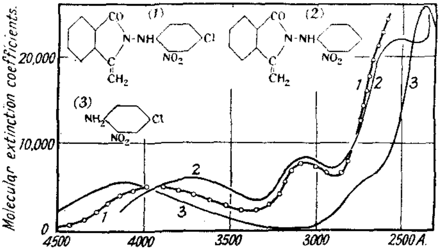
ment of the absorption bands may be expected. Stilbene and the methylstilbenes illustrate this point (Ley and Rinke, *Ber.*, 1923, **56**, 771; Ley, " Handbuch der Physik," **21**, **121**).

		$\lambda_{max.}$, A.
Stilbene	$C_6H_5\cdot CH{:}CH\cdot C_6H_5$	2950
α-Methylstilbene	$C_6H_5\cdot C(CH_3){:}CH\cdot C_6H_5$	2690
αβ-Dimethylstilbene	$C_6H_5\cdot C(CH_3){:}C(CH_3)\cdot C_6H_5$	2400
p-Methylstilbene	$C_6H_5\cdot CH{:}CH\cdot C_6H_4\cdot CH_3(p)$	2950

The fact that in the 4′-nitrophenylphthalazones the 1-methyl group has no influence on the absorption in the case of the 4-one, whilst the 4-methyl group has a marked hypsochromic effect in the 1-one, must be ascribed to a steric effect of the methyl group in the latter case. This difference is consistent with the apparent structure of the two types of compounds, for in the 1-one the 4-methyl group is directly attached to the chromophoric system responsible for the near ultra-violet band (see below), whereas this is not so with the 1-methyl group in the 4-one (cf. II and IV).

The absorption curves of the four analogous 4′-chloro-2′-nitro-compounds are reproduced in Fig. 4. Again the 4-ones are less strongly absorbing in the near ultra-violet than the 1-ones and the introduction of the 1-methyl group into the 4-one results in little difference in the absorption, whereas the 4-methyl group in the case of the 1-one causes a large hypsochromic effect (4030 A. ⟶ 3430 A.).

FIG. 5.



1. ○——○ 2-(4′-*Chloro-2′-nitrophenylamino*)-3-*methylene*iso*indolinone*.
2. – – – – 2-(2′-*Nitrophenylamino*)-3-*methylene*iso*indolinone*.
3. ———— 4-*Chloro-2-nitroaniline*.

When the absorption curve of 4′-nitro-3-phenylphthalaz-1-one (Fig. 3) is compared with that of the 4′-chloro-2′-nitro-analogue (Fig. 4), it is seen that the long-wave band is displaced to longer wave-lengths (3670 A. ⟶ 4030 A.). These absorption bands must therefore be due to the chromophore of the nitroarylamine residue, the change in location being associated with the change in the position of the nitro-group from para- to ortho-. This is clearly indicated by the close analogy between the absorption of these particular phthalazones and that of *p*- and *o*-nitroaniline (Morton and McGookin, J., 1934, 901):

	$\lambda_{max.}$, A.	$\epsilon_{max.}$
4′-Nitro-3-phenylphthalaz-1-one	3670	9,600
p-Nitroaniline	3740	15,000
4′-Chloro-2′-nitro-3-phenylphthalaz-1-one	4030	4,900
o-Nitroaniline	4040	5,400

The absorption curves of 2-(2′-nitrophenylamino)-3-methylene*iso*indolinone (VI; R = 2′-nitrophenyl) and the 4′-chloro-2′-nitro-analogue are reproduced in Fig. 5.

In compounds of the complexity of those at present under discussion, it is difficult to associate the various absorption bands with particular chromophoric groups in the molecule with any degree of certainty. Nevertheless, from the foregoing evidence it is clear that the complex chromophore formed by substituting hydrogen in the nitroarylamine is responsible for much of the absorption of the 1-ones. As a further confirmation the absorption of 4-chloro-2-nitro-aniline was examined (Fig. 5). The long-wave absorption band is very similar in location.

intensity, and general shape to the bands of 4′-chloro-2′-nitro-3-phenylphthalaz-1-one (Fig. 4) and 2-(4′-chloro-2′-nitrophenylamino)-3-methylene*iso*indolinone :

	$\lambda_{max.}$, A.	$\epsilon_{max.}$
4-Chloro-2-nitroaniline	4100	5400
4′-Chloro-2′-nitro-3-phenylphthalaz-1-one	4030	4900
2-(4′-Chloro-2′-nitrophenylamino)-3-methylene*iso*indolinone	3950	5000

The evidence that the near ultra-violet absorption of 4-chloro-2-nitroaniline persists in the above *iso*indolinone being accepted, the new molecular environment of the chromophoric group must displace the maximum from 4100 A. to 3950 A. The very similar absorption of the corresponding 1-one has already been shown to be closely comparable with that of *o*-nitroaniline (*vide supra*), but the fact that, despite the similarity of its molecular environment with that of the *iso*indolinone, it has its maximum displaced by 80 A. to longer wave-lengths can be attributed to the additional double bond with which the chromophore is conjugated (3950 A. ⟶ 4030 A.; cf. II). As the absorption of 4-chloro-2-nitroaniline does not persist in the derived 4-ones (Fig. 4), other groups in the structurally different molecules of this series of compounds must cause the displacement of the absorption to shorter wave-lengths.

The authors are indebted to Alliance Colour and Chemical Co., and Imperial Chemical Industries, Ltd. (Dyestuffs Group), for gifts of chemicals.

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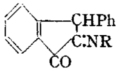
22. *Autoxidation Phenomena and Valency Tautomerism * in the Indone Series.*

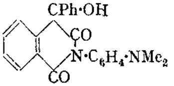
By ALEXANDER SCHÖNBERG and ROBERT MICHAELIS.

(A) IN view of the important part played by autoxidation processes in many branches of chemistry, a recent paper by Pfeiffer and de Waal (*Annalen*, 1935, **520**, 185) attracts special interest on account of the description of an autoxidation process which is without analogy.

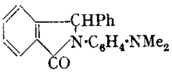
These workers claim that, although the colourless oxime (I) and the corresponding deep blue-violet anil (II) are stable in air, yet the deep blue-violet *p*-dimethylaminoanil (III) (which is stable in the solid state) is oxidised in solution to an *iso*quinoline derivative (IV), which reacts with alkalis to form (V). They point out that the anil (II) is oxidised by hydrogen peroxide to a new compound for which they propose the formula (VI) or (VII).



(I) R = OH
(II) R = Ph
(III) R = $C_6H_4 \cdot NMe_2$

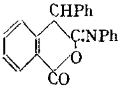


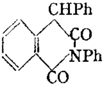
(IV.)



(V.)

(VI.)





(VII.)

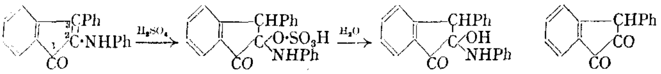
In criticism of Pfeiffer and de Waal's conclusions, it may be pointed out that the sensitivity of (III) towards oxygen (which is as great as that of triphenylmethyl) is not in accordance with their formula; and further, that the transformations of (III) ⟶ (IV), (IV) ⟶ (V), and (II) ⟶ (VI) or (VII), *under the experimental conditions given, are not* supported by evidence from analogous reactions. Moreover, it is highly improbable that the

* Compare A. Schönberg, *Ber.*, 1931, **64**, 2323; 1934, **67**, 633; *Annalen*, 1935, **518**, 299; *Trans. Faraday Soc.*, 1936, **32**, 514; *Naturwiss.*, 1936, 620. For the meaning of "valency tautomerism" compare Wieland (*Ber.*, 1920, **53**, 1318; 1922, **55**, 1806).

oxime of a 1 : 2-diketone (in our case IX) should be colourless while the anil of the same diketone is deep blue-violet.

Although each of these difficulties may be overcome with the help of special hypotheses, it appeared to us important, in connexion with the work of one of us (Sch.) on the autoxidation of rubrene, to reinvestigate the phenomena observed by Pfeiffer and de Waal. Although the experimental evidence of their excellent work has been completely confirmed by us (as far as reinvestigated), we have arrived at an essentially different explanation, as a result of further investigation.

(B) We prefer to formulate the alleged anil (II) (obtained by the action of nitrosobenzene on XIX) as 2-anilino-3-phenylindone (VIII).* This formula completely explains the properties and colour of the compound for the following reasons: (1) the substance is shown to possess one active hydrogen atom by Zerewitinoff analysis. [The result of the Zerewitinoff analysis would also be in accordance with formula (III*a*) (footnote, below), which is, however, excluded by the fact that the substance is not acted upon by diazomethane.] (2) The ease with which (VIII) takes up one atom of oxygen in the presence of hydrogen peroxide is analogous to the behaviour of 2 : 3-diphenylindone and of 3-phenyl-2-ethylindone (Weitz and Scheffer, *Ber.*, 1921, **54**, 2327; de Fazi and Pirrone, *Gazzetta*, 1930, **60**, 277, 283). (3) The conversion of (VIII) into (IX), accomplished by Pfeiffer by treatment with concentrated sulphuric acid, followed by hydrolysis, we believe to take place as follows, and to be dependent upon the well-known tendency of the double bond in indones to undergo addition reactions with ease. The phenomenon can also be explained by prototropic change with

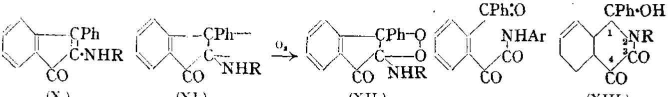


(VIII.) (IX.)

subsequent ψ-salt formation and hydrolytic splitting. (4) The change from (VIII) to the dioxime of (IX) is formulated in a similar manner. In addition to the reaction between the carbonyl group and hydroxylamine, one molecule of the latter is added at the double bond between C_2 and C_3 and then a molecule of aniline is split off. (5) The blue-violet colour of the compound is in conformity with the formula suggested (VIII) [compare the red colour of 2 : 3-diphenylindone (VIII, with Ph in place of NHPh)].

(C) The blue-violet product of the condensation between 3-phenylindanone (XIX) and *p*-nitrosodimethylaniline we consider to be 2-*p*-dimethylaminoanilino-3-phenylindone (X; R = $C_6H_4{\cdot}NMe_2$) (according to Pfeiffer and de Waal, it is III).

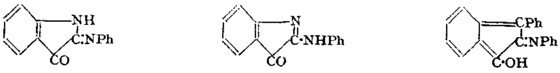
This compound behaves in a similar fashion to (VIII) towards Zerewitinoff analysis and diazomethane. The above considerations of the relation between colour and constitution also apply to (X). The oxidation of this compound by air, we consider to take place as follows and therefore the oxidation product to be 1-hydroxy-3 : 4-diketo-2-*p*-dimethylaminophenyl-1-phenyl-1 : 2 : 3 : 4-tetrahydro*iso*quinoline (XIII; R = $C_6H_4{\cdot}NMe_2$):



(X.) (XI.) (XII.) (XIII.)

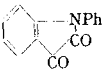
R = $C_6H_4{\cdot}NMe_2$

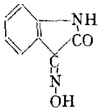
* It is possible that the primary product in the condensation is (II), which could not be isolated, and changed to (VIII). Compare the following change of an anil (I*a*) into an anilino-compound (II*a*) when heated (Pummerer, *Ber.*, 1911, **44**, 339):

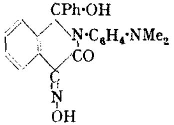


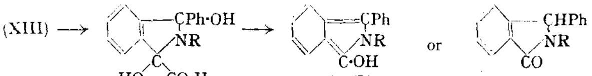
(I*a*.) (II*a*.) (III*a*.)

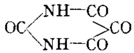
The formula of (XIII) is based on the following grounds : (1) The orange colour is in conformity with the proposed constitution (*N*-phenylisatin, XIV, is orange). (2) By Zerewitinoff analysis, (XIII) is shown to have one active hydrogen atom (compare Pfeiffer, *loc. cit.*). (3) It yields under mild conditions the oxime (XVI), whose formation is not in accordance with Pfeiffer's formula (IV). (4) The alteration in colour from (XIII) (orange) to (XVI) (yellow) is analogous to the change from isatin (orange) to its β-oxime (XV) (yellow). (5) The transformation (XIII) ⟶ (XVII) by the action of alkalis we consider to be a " benzilic acid rearrangement," followed by elimination of carbon dioxide and water [compare conversion of (XVII) ⟶ (XVIII) (Biltz, Heyn, and Bergius, *Annalen*, 1916, **413**, 68) under the influence of alkalis]. But we do not want to exclude the possibility that the action of alkali on (XIII) can lead to a cleavage of the six-membered ring, followed by ring closure to a five-membered system.

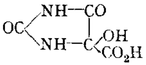

(XIV.)

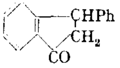

(XV.)


(XVI.)


(XVII.)
R = $C_6H_4 \cdot NMe_2$


(XVII.)


(XVIII.)


(XIX.)

(D) The abnormal sensitivity of (X) to oxygen (we found it to be as unstable in oxygen as triphenylmethyl even in the dark) cannot be explained by the classical theories of chemical structure. In order to correlate the formula with the chemical properties it may be supposed that (X) in solution can act as its valency-tautomeric form (XI), which adds on oxygen by reason of its two tervalent carbon atoms.

(X) in the solid state is stable towards oxygen. This may be explained by either of the following hypotheses : (1) only the normal form is present in the solid; (2) both forms are present, but a thin oxidised layer is formed on the surface of the crystal, hindering further oxidation.

Whether one can demonstrate by electromagnetic measurements the presence of an equilibrium (X) $\rightleftharpoons$ (XI) will depend on whether the equilibrium is driven so far to the right that the paramagnetic influence of (XI) may be demonstrated, since the limits of error in this type of measurement are large (cf. Sugden, *Trans. Faraday Soc.*, **1934**, **30**, 24; Eistert, *Ber.*, 1936, **69**, 2397; Müller, Müller-Rodloff, and v. Bunge, *Annalen*, 1935, **520**, 235; **521**, 89; Schönberg, *Trans. Faraday Soc.*, 1936, **32**, 520). At the present stage of chemical knowledge it is impossible to say why (X; R = $C_6H_4 \cdot NMe_2$ or $C_6H_4 \cdot OMe$)* can react in valency-tautomeric forms, whereas (X; R = Ph) so far as is known cannot. A familiar phenomenon occurs in the following case : Tetraphenylhydrazine is only slightly dissociated, but replacement of the phenyl by *p*-dimethylaminophenyl or anisyl groups produces highly dissociated substances (Wieland, *Ber.*, 1915, **48**, 1078). Compare also nitrosobenzene, which is dimeric and colourless, in the solid state, monomeric and green in

* The blue-violet compound unstable towards oxygen which is described by Pfeiffer and de Waal as (I) is 2-*p*-methoxyanilino-3-phenylindone (X), and the product obtained from it by oxidation in air is (XIII). R = $C_6H_4 \cdot OMe$ in all three formulæ.

solution, and *p*-nitrosoanisole and *p*-nitrosodimethylaniline, which are green and monomeric in solution *and* in the solid state.

EXPERIMENTAL.

2-Anilino-3-phenylindone (VIII).—Estimation of active hydrogen by Zerewitinoff's method gives 0·33% ($C_{21}H_{15}ON$ requires for one active hydrogen atom, 0·34%).

Behaviour with diazomethane. The substance (1 mol.), dissolved in ether and added to an ethereal solution of diazomethane (6 mols.), is kept for 2 hours at 0° and for 18 hours at room temperature. It is then recovered unchanged.

2-p-*Dimethylaminoanilino-3-phenylindone* (X).—Active-hydrogen estimation (Zerewitinoff's method), found 0·32% ($C_{23}H_{20}ON_2$ requires for one active hydrogen atom, 0·29%).

Importance of light in oxidation by air. The material (0·1 g.) in methyl alcohol (100 c.c.) is boiled for 2 mins. and kept over-night, in the dark. The originally green solution becomes orange and crystals of (XIII) separate. Therefore oxidation by air takes place even when light is excluded.

(X), dissolved in benzene, reacts instantaneously with a benzene solution of bromine with change of colour.

Action of diazomethane on (X). The same experimental conditions are used as above except that in this case air is excluded. After 20 hours, the ether is removed, and the residue dissolved in methyl alcohol and exposed to oxidation by air. (XIII) is formed in such quantity as to show that very little or no reaction takes place with diazomethane.

Action of hydroxylamine. To 0·5 g. of (XIII) in 300 c.c. of warm alcohol is added a solution of hydroxylamine hydrochloride (10 mols.) and sodium acetate in the minimum amount of water. During the addition the orange-coloured solution turns yellow. Sodium chloride soon begins to separate. After 14 hours, the liquid is concentrated to about 20 c.c. and water is added till no more oily material separates. The aqueous alcoholic solution, made alkaline with ammonia, is kept for 1½ hours and the precipitate is then filtered off, washed well with water, and dried in a desiccator (yield, 0·45 g.). The substance is dissolved in ether, and light petroleum (b. p. 80—100°) added till a slight turbidity is produced. After reprecipitation as above, the purified material (XVI) forms light yellow, refractive crystals which redden and sinter at 180° and melt at 192° (Found: C, 71·3; H, 5·4; N, 10·9. $C_{23}H_{21}O_3N_3$ requires C, 71·3; H, 5·4; N, 10·8%).

Action of methyl iodide. To 10 c.c. of methyl iodide boiling in an atmosphere of nitrogen is added 1 g. of (X), which is completely dissolved. After standing for a short time, a precipitate appears. The mixture is then warmed for 2 hours and cooled, and 40 c.c. of boiled absolute ether added. The violet crystals which form are collected after 12 hours, washed with ether, and dried in a vacuum (yield, 1·4 g.). The *substance* is purified by boiling it for 20 minutes with acetone. The now uniformly crystalline material is washed with acetone and dried. It forms deep blue-violet crystals decomposing at 226°. It is much more stable to oxygen than (X), difficultly soluble in cold water, chloroform and acetone, soluble in hot water, and very soluble in warm ethyl alcohol (Found: C, 59·8; H, 4·9; N, 5·9; I, 27·1. $C_{24}H_{23}ON_2I$ requires C, 59·7; H, 4·8; N, 5·8; I, 26·3%).

SUMMARY.

The reaction (III) ⟶ (IV) described by Pfeiffer and de Waal is to be replaced by the reaction (X) ⟶ (XI) ⟶ (XIII). Corresponding corrections in relation to other reactions described by Pfeiffer and de Waal are suggested.

The valency tautomerism between (X) and (XI) is discussed.

The authors wish to thank the Chemical Society for a grant to one of them (Schönberg) and Prof. G. Barger, F.R.S., for his hospitality.

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23. *Decomposition Reactions of the Aromatic Diazo-compounds. Part I. Evidence for Non-ionic Reaction.*

By William A. Waters.

Grieve and Hey (J., 1934, 1799, 1966) brought forward strong experimental evidence for the view that the decomposition of the aromatic diazo-compounds was non-ionic in character and gave rise to the transient existence of free aryl radicals. In particular they showed that, in a series of solvents, the rate of decomposition of benzene *iso*(*anti*)-diazoacetate was influenced but slightly by the nature of the solvent, and that, in the preparation of derivatives of diphenyl by the reactions of Bamberger and Gomberg, a substituting phenyl group gave invariably a para-substituted product, not acting therefore either as a kationoid or as an anionoid reagent.

The possibility of this non-ionic decomposition ($Ph{\cdot}N_2{\cdot}X \longrightarrow Ph{\cdot} + N_2 + {\cdot}X$, not $Ph^+ + N_2 + X^-$ (compare Bradley and Robinson, J., 1928, 1312) in many of the familiar diazo-reactions had independently occurred to the author in 1931 (*Proc. Durham Phil. Soc.*, 1932, **8**, 459) when endeavouring to collect information concerning the reactions of the neutral free radicals (compare Waters, "Physical Aspects of Organic Chemistry," 1935, Chap. VII), for it seemed unlikely that the decompositions of benzeneazotriphenylmethyl (Wieland, *Ber.*, 1922, **55**, 1816) and azomethane (Ramsperger, *J. Amer. Chem. Soc.*, 1927, **49**, 912, 1495; Leermakers, *ibid.*, 1933, **55**, 3499) could be unique.

With the concurrence of Dr. Hey the author commenced experimental work to substantiate this hypothesis of non-ionic fission of nitrogen gas from the aromatic diazo-compounds, and, in consequence, a further study has been made of the decomposition of benzene *iso*(*anti*)-diazoacetate, prepared as its labile tautomer *N*-nitrosoacetanilide. It was obvious that, if free neutral phenyl radicals could be produced by the decomposition of a diazo-compound in the liquid phase, one would be dealing with an extremely reactive substance, liable to interact with and decompose the first molecule it encountered. Consequently any reaction occurring in a solvent would be principally an interaction of a phenyl radical with a solvent molecule, no matter what other dissolved substances might be added, and hence but little new information might be drawn from re-examining any earlier work on the decomposition of diazo-compounds in aqueous solution. Dry benzene diazoacetate was therefore prepared and allowed to decompose in a number of anhydrous solvents at room temperature. With all the liquids examined as yet, it reacts vigorously, yielding to the extent of 5—40% a simple aromatic compound, together with a complex tar.

In *n*-hexane and in *cyclo*hexane the diazoacetate was practically insoluble, but nevertheless, decomposition in suspension yielded small quantities of *benzene* in each case. Benzene was also a product of the decomposition in solutions in diethyl ether, dioxan, acetone, ethyl acetate, acetonitrile, and acetic anhydride. With the first four of these solvents acetic acid and an aldehyde were also produced. It therefore appeared that the non-ionic reaction $Ph{\cdot} + H{\cdot}R \longrightarrow Ph{\cdot}H$ was a regular occurrence in hydrogen-containing solvents, and need not necessarily be attributed to the action of a reducing agent, as is customarily done when explaining the decomposition of a benzenediazonium salt in ethyl-alcoholic solution. Moreover the decomposition in acetic anhydride also yielded *carbon dioxide*, which can only be attributed to the transient formation of the neutral acetate radical,

$$ {\cdot}O{\cdot}CO{\cdot}CH_3 \longrightarrow CO_2 + {\cdot}CH_3 \ (\longrightarrow CH_3{\cdot}CH_3) $$

since an acetate anion, $(O{\cdot}CO{\cdot}CH_3)^-$, never loses carbon dioxide at room temperature, except on discharge at an anode.

With both methyl and ethyl iodides there was produced iodobenzene; with ethyl bromide and with bromoform there was produced bromobenzene, and with chloroform and carbon tetrachloride there was produced chlorobenzene. Thus the reaction $Ph{\cdot} + Hal{\cdot}R \longrightarrow Ph{\cdot}Hal$ has beeen substantiated. The decomposition in carbon tetrachloride solution again yielded carbon dioxide in quantity.

Carbon dioxide was also evolved when benzene diazoacetate decomposed in carbon disulphide solution, and in this case the other simple reaction product was diphenyl di-

sulphide, Ph·S·SPh. A solution of iodine in carbon disulphide, however, yielded iodobenzene in 40% yield. This may conceivably be produced by a direct union of free radicals: $2Ph\cdot + I_2 = 2PhI$.

Further it has been shown that, during the decomposition of benzene diazoacetate in the non-polar solvents carbon disulphide and carbon tetrachloride, metallic elements may be attacked. In carbon disulphide solution zinc, iron, copper, lead and antimony all yielded products soluble in water—their acetates principally. Even in the presence of an excess of calcium carbonate, zinc, iron, copper and lead were attacked, so that the solution of the metal is not to be explained as an attack by acetic acid molecules in presence of air. When calcium carbonate was used, however, the aqueous extracts of the decomposition products all contained calcium ions, so that some acetic acid molecules must be produced by the self-interaction of products of the benzene diazoacetate decomposition, *e.g.*,

$$\cdot O\cdot CO\cdot CH_3 + HR \longrightarrow HO\cdot CO\cdot CH_3.$$

Silver foil was not attacked during the decomposition of benzene diazoacetate in a carbon disulphide solution containing calcium carbonate.

In carbon tetrachloride solution tin, copper, mercury and probably bismuth were attacked, giving water-soluble products. The mercury yielded mercurous and mercuric chlorides and also phenylmercuric chloride. In this connection it may be pointed out that McClure and Lowy (*J. Amer. Chem. Soc.*, 1931, **53**, 319) have found that even in aqueous solution benzenediazonium chloride yields this product if allowed to decompose in a solution in which are suspended, by rapid stirring, globules of metallic mercury.

All these reactions with metals, many of which are rather inert, recall in a most striking manner Paneth's tests for the free radicals. Indeed practically without exception the reactions enumerated above are typical of free neutral radicals, and could not occur if a phenyl kation or a phenyl anion was a reaction product. Moreover there has already been recorded one early reaction of this same type which could hardly be attributed to an ionic change. Möhlau and Berger (*Ber.*, 1893, **26**, 1994) allowed dry benzenediazonium chloride to decompose in pyridine and obtained α- and γ-phenylpyridines. Phenyl kation and chloride anion would inevitably have attacked the nitrogen atom of the pyridine and yielded instead phenylpyridinium chloride.

The non-ionic decomposition of benzene diazoacetate may well be typical of all the decomposition reactions of the aromatic diazo-compounds, for a search of the literature does not reveal any contradictory evidence. The hypothesis will greatly amplify, but not in essentials contradict, the theories propounded by Hantzsch, which, in many aspects, remain unproved. Hence it would appear that a careful reinvestigation of the diazo-reactions in the light of the free-radical hypothesis might shed considerable light upon the mechanisms of the reactions of Sandmeyer and Gattermann, in which a copper compound catalytically alters the normal course of decomposition in aqueous solution. Further, the production of neutral aryl radicals, at will, in solutions, is somewhat of a novelty, and in view of their intense reactivity it would now seem possible to extend our knowledge of the chemistry of the free radicals by further studies of decompositions of aryl diazo-compounds in non-aqueous solutions. The experimental work is therefore being continued.

The author wishes to thank Dr. Hey for agreeing to his entry into this field of experimental work so as to search independently for evidence of non-ionic reactions. He has maintained throughout constant communication with Dr. Hey and his results, arrived at in the laboratories at Durham, independently corroborate the work carried out in Manchester. At the author's suggestion Dr. Hey has very kindly repeated and confirmed in his laboratory the critical reactions demonstrating the evolution of carbon dioxide in solutions in acetic anhydride, carbon tetrachloride and carbon disulphide, and also the interactions in carbon disulphide and carbon tetrachloride solutions with metallic zinc, copper, and mercury. In conclusion the author hopes that this friendly interchange of information will continue to be equally fruitful to both investigators in the future.

EXPERIMENTAL.

The benzene *iso*diazoacetate (nitrosoacetanilide) used in the following reactions was prepared as described by Grieve and Hey (*loc. cit.*) and dried for 2 days over calcium chloride

in a vacuum desiccator. Specimens kept for a longer time decomposed rapidly, and in one instance exploded.

(I) *Decomposition in Liquids containing Hydrogen.*—(i) n-*Hexane.* Gases were gradually evolved at room temperature from benzene diazoacetate (7 g.) covered with *n*-hexane (15 g., B. D. H. " pure for spectroscopy ") in a water-cooled flask. After 6 days the hexane was distilled on the water-bath and shown to contain benzene by (*a*) nitration, which yielded some *m*-dinitrobenzene, m. p. and mixed m. p. 91°, and (*b*) by a very sensitive conversion into diphenyliodonium iodide recently discovered in these laboratories by Professor Irvine Masson.* The residue was distilled in steam, but yielded no diphenyl.

(ii) cyclo*Hexane.* The above reaction was repeated with *cyclo*hexane free from benzene. After 8 days the portion distilling below 100° gave positive tests for benzene by both reactions.

(iii) *Diethyl ether.* Gases were evolved immediately from benzene diazoacetate (6 g.) dissolved in sodium-dried ether (50 c.c.) in a water-cooled flask under a reflux condenser and the smell of acetaldehyde was soon noticeable. After a day, since reaction had ceased, benzene-free hexane (20 c.c.) was added as a vehicle for the collection of any benzene, and the mixture was distilled on the water-bath. The distillate gave a very strong reaction with Schiff's reagent, a positive iodoform test, and reacted with 2 : 4-dinitrophenylhydrazine. The hydrocarbon layer remaining after repeated washing with water gave strong positive tests for the presence of benzene by both reactions (*a*) and (*b*) above.

(iv) *Dioxan.* A solution of benzene diazoacetate in dioxan was allowed to decompose for 4 days and then, by addition of hexane, distillation, etc., as in (iii) above, was shown to contain a considerable quantity of benzene.

(v) *Acetone.* A solution of benzene diazoacetate in A.R. acetone was allowed to decompose for a week. After addition of hexane the distillate below 100° gave a positive test with Schiff's reagent, and the hydrocarbon fraction, after washing with sodium bisulphite solution, contained benzene, which had been produced in not less than 50% yield.

(vi) *Acetonitrile.* In this solvent again benzene formed the principal reaction product. There was no evidence of the formation of benzonitrile.

(vii) *Ethyl acetate* (compare Grieve and Hey, *loc. cit.*). Benzene diazoacetate on decomposition in dry ethyl acetate solution soon produced acetaldehyde. After addition of hexane the distillate below 100° gave a positive reaction with Schiff's reagent, and the hydrocarbon layer contained benzene, produced in about 50% yield. The residue not volatile at 100° was distilled in steam and yielded acetic acid and traces of phenol, but neither phenyl acetate nor diphenyl.

(viii) *Acetic anhydride.* Benzene diazoacetate (6 g.), dissolved in acetic anhydride (30 g.), was allowed to decompose in a water-cooled flask fitted with a reflux condenser, from which the evolved gases were led through a fresh solution of baryta. A thick precipitate of barium carbonate soon indicated the presence of carbon dioxide as a reaction product.** After a week hexane (20 c.c.) was added, and the mixture distilled on the water-bath. The distillate gave positive tests for the presence of benzene by both reactions (*a*) and (*b*) above.

(II) *Decomposition in Liquids containing Halogens.*—(i) *Methyl iodide.* Benzene diazoacetate (6 g.) was allowed to decompose in methyl iodide (20 g.) in a water-cooled flask, and after 3 days the excess of solvent was removed by distillation. On distilling the residue in steam there was obtained iodobenzene (0·8 g.), b. p. 187°, identified by conversion into *p*-iodonitrobenzene, m. p. 173—174° alone or mixed with an authentic specimen.

(ii) *Ethyl iodide.* The same quantities being used as in the preceding experiment, from ethyl iodide there was obtained 0·3 g. of iodobenzene, which was identified in a similar manner.

(iii) *Ethyl bromide.* Benzene diazoacetate (7 g.) when decomposed in ethyl bromide (30 g.) gave bromobenzene (0·3 g.), which was separated by steam distillation and identified by conversion into *p*-bromonitrobenzene, m. p. and mixed m. p. 126°.

(iv) *Bromoform.* Benzene diazoacetate (6 g.) was decomposed in bromoform (30 g.) which had been shaken with concentrated sulphuric acid and then freshly distilled. The product from steam distillation was saponified with alcoholic potash, and the unattacked residue of bromobenzene (0·6 g.) identified by conversion into *p*-bromonitrobenzene.

(v) *Chloroform.* Benzene diazoacetate (7 g.) after decomposition in 50 c.c. of chloroform, purified by shaking with concentrated sulphuric acid and distillation, gave 0·7 g. of a colourless oil, b. p. *ca.* 143°, which smelt strongly of chlorobenzene and on nitration, gave a gummy product which reacted with piperidine.

(iv) *Carbon tetrachloride.* Decomposition of 8 g. of benzene diazoacetate in 80 g. of carbon

* To be published shortly.

tetrachloride gave 1·5 c.c. of a liquid, b. p. 130—160°, containing chlorobenzene. This was nitrated, giving a product, m. p. 46—47° (after crystallisation from methyl alcohol), raised slightly in admixture with authentic 2 : 4-dinitrochlorobenzene. The crude nitration product reacted with piperidine, and, with aniline, it gave 2 : 4-dinitrodiphenylamine, m. p. and mixed m. p. 156—157°. Another portion of benzene diazoacetate on decomposition in carbon tetrachloride was shown to give carbon dioxide in quantity by passing the evolved gases through a fresh baryta solution, from which barium carbonate was soon deposited.** From this reaction mixture the excess of carbon tetrachloride was removed by distillation on the water-bath, and the residue was then hydrolysed for 3 hours with alcoholic potash. The alkaline product was examined for the presence of benzoic acid, but none could be found. Hence benzotrichloride does not seem to be a reaction product.

(vii) *Phosphorus trichloride.* Benzene diazoacetate was slowly added in very small portions to phosphorus trichloride in a basin. It reacted at once, giving initially a white precipitate, which was presumably benzenediazonium chloride, since it gave an azo-dye with β-naphthol. Eventually a tarry mass was formed, which, after treatment with water, yielded acetanilide, m. p. 114°. Chlorobenzene did not appear to be formed.

(III) *Decomposition in Carbon Disulphide.*—40 G. of benzene diazoacetate were dissolved in 300 c.c. of carbon disulphide (which had been purified by shaking with anhydrous copper sulphate and distillation) in a water-cooled flask fitted with a reflux condenser, from which the evolved gases were led through a fresh solution of baryta protected from the air by a guard tube. Formation of carbon dioxide was apparent after 15 minutes,** and soon there was a thick deposit of barium carbonate. After a week reaction had ceased, and the excess of solvent was then distilled off on the water-bath. The red tarry residue was extracted four times with successive portions (300 c.c. each) of light petroleum (b. p. 60—80°) and these solutions were evaporated as far as possible on the water-bath. The residue thus obtained was similarly extracted with light petroleum (b. p. 40—60°), and this solution after concentration gave an orange-red gum which solidified almost completely on freezing. This, crystallised repeatedly from methyl alcohol–ether and finally from methyl alcohol alone, gave 8 g. of colourless needles, m. p. 61·5°, which were proved to be diphenyl disulphide (Found : S, 29·7. Calc., 29·4%). A portion of the product was boiled with alcoholic potash, and the solution after acidification yielded thiophenol on steam distillation, from which were prepared lead, copper, mercury, and silver salts. Diphenyl disulphide was also synthesised from thiophenol, and the specimen thus obtained had a melting point unaltered by admixture with the specimen from the decomposition of the benzene diazoacetate.

No other reaction product could be isolated in appreciable quantity from the tarry residue by extraction with other solvents.

Decomposition of benzene diazoacetate in a solution of sulphur in carbon disulphide yielded no reaction product other than that isolated from the pure solvent.

(IV) *Reaction with Iodine in Carbon Disulphide.*—8 G. of benzene diazoacetate and 8 g. of iodine were dissolved in 50 c.c. of purified carbon disulphide, and the mixture was allowed to decompose in a water-cooled flask under a reflux condenser. After 6 days the carbon disulphide was distilled off on the water-bath, and the residue treated with water and steam distilled. After the distillate had been decolourised with sodium sulphite, the remaining heavy oil was extracted with ether, dried, and fractionated. 3·3 G. of iodobenzene, b. p. 186—191°, were thus obtained, and identified by conversion into *p*-iodonitrobenzene, m. p. and mixed m. p. 173°.

(V) *Reaction with Metals in Carbon Disulphide Solution.*—To separate portions (6 g.) of benzene diazoacetate, dissolved in dry carbon disulphide (30 c.c.) were added : (*a*) 10 g. of iron filings, (*b*) 10 g. of zinc dust,** (*c*) 10 g. of copper powder,** (*d*) 20 g. of lead filings, (*e*) 15 g. of powdered antimony, (*f*) 20 g. of mercury. The mixtures were allowed to decompose for 2 days in water-cooled flasks under reflux condensers, and were shaken frequently. The excess of solvent was then evaporated from each solution on the water-bath, and the residues were shaken for 2 minutes with cold water and filtered. The clear aqueous extracts in each instance contained acetate ions in quantity. In addition the solution from (*a*) contained much ferrous and some ferric ions, from (*b*) zinc ions,** from (*c*) cupric ions,** from (*d*) lead ions, produced in considerable quantity in every case. From (*e*) the aqueous extract contained no antimony compound, but when the residue was warmed for 2 minutes with aqueous ammonium tartrate and filtered, the colourless filtrate gave with hydrogen sulphide a heavy black precipitate containing antimony, verified by positive Marsh and Gutzeit tests, and by the formation of a metallic bead on fusion. From mixture (*f*) no mercury salts were obtained.

Since it was possible in some cases that the metal had been attacked by acetic acid—a likely product of self-decomposition of benzene diazoacetate—rather than by free radicals, the reactions (*a*) to (*d*) were repeated with the addition of 6 g. of dry precipitated chalk to each mixture. Strong positive tests for ferrous, ferric, zinc, cupric, lead, and acetate ions were still given by the cold aqueous extracts. In addition, however, each solution contained calcium ions, showing that acetic acid also must be a reaction product.

A mixture of 6 g. of benzene diazoacetate, 6 g. of precipitated chalk, 30 c.c. of carbon disulphide, and 4 g. of pure silver foil was also allowed to decompose. After treatment as described above, the aqueous extract contained calcium and acetate ions in quantity but no silver ions, and the recovered foil showed no signs of attack.

(VI) *Reaction with Metals in Carbon Tetrachloride Solution.*—To separate portions of benzene diazoacetate (6 g.), dissolved in carbon tetrachloride (20 c.c.), were added: (*a*) 6 g. of copper** powder, (*b*) 12 g. of tin powder, (*c*) 12 g. of powdered bismuth, and (*d*) 20 g. of mercury.** The mixtures were allowed to decompose for 2 days in water-cooled flasks under reflux condensers and were shaken frequently. Mixture (*d*) soon became turbid owing to the formation of an insoluble white substance. After removal of the excess of solvent by distillation on the water-bath each mixture was shaken for 2 minutes with warm water and filtered. From (*a*) the extract contained cupric,** chloride, and acetate ions; from (*b*) stannous and chloride ions, and from (*d*) chloride ions in quantity together with a trace of mercuric ions. From (*c*) no metallic ions were found in the aqueous extract, but the residue, after warming for 2 minutes with 2*N*-hydrochloric acid, yielded a colourless solution containing bismuth ions in quantity. Another portion of bismuth metal was warmed with 2*N*-hydrochloric acid for the same length of time and only a faint trace of the metal was dissolved by the acid.

The reaction mixture (*d*) was treated with successive portions of warm rectified spirit on a filter-paper, and eventually there remained globules of mercury and a white insoluble powder. This was extracted with hot benzene until no more would dissolve. The white powder then remaining blackened instantly on treatment with ammonia and dissolved in aqua regia to give a solution containing mercuric ions. It was thus presumed to be mercurous chloride. The benzene extract was concentrated to small bulk; colourless plates then crystallised. After further crystallisation they melted at 252°, burnt with a smoky flame, and were found to contain both mercury and chlorine. Hence they must consist of phenylmercuric chloride (m. p. recorded 251°).**

The experiments marked ** have been repeated by Dr. D. H. Hey in his laboratory at Manchester, and the results confirmed in all details.

UNIVERSITY SCIENCE LABORATORIES, DURHAM. [*Received, November 18th, 1936.*]

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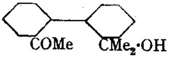
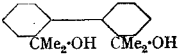
24. *Some 2 : 2'-Derivatives of Diphenyl.*

By DOROTHY E. COOK and E. E. TURNER.

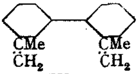
WHEN diphenoyl chloride is allowed to react with excess of methylmagnesium iodide, two products are formed: *2-acetyl-2'-α-hydroxy*iso*propyldiphenyl* (I) and *2 : 2'-di-α-hydroxy*iso*propyldiphenyl* (II).



(I.)



(II.)



(III.)

Under similar conditions, methyl diphenate and 2 : 2'-diacetyldiphenyl react with the same Grignard reagent to give mainly the glycol (II) (cf. Schenk and Brauns, *Ber.*, 1915, **48**, 716; Tschitschibabin and Ssergejeff, *Ber.*, 1926, **59**, 654). The alcohol-ketone (I) reacts with excess of the Grignard reagent to give (II), but the yield is poor.

The glycol (II) undergoes dehydration with great readiness, and it was found that phosphorus tribromide, or this substance mixed with phosphorus pentabromide at temperatures up to 100°, or dry hydrogen chloride at 150°, gave no di-α-halogeno*iso*propyldiphenyl,

but only 2 : 2'-*di-α-methylethenyldiphenyl* (III). 2 : 2'-Dihydroxybenzhydryldiphenyl (Tschitschibabin and Ssergejeff, *loc. cit.*) was found to be unaffected when heated in a current of dry hydrogen chloride at 200°.

2 : 2'-Diacetyldiphenyl would be expected to undergo smooth ωω'-dibromination. We find that carefully controlled interaction of the diketone with two molecular proportions of bromine in glacial acetic acid, in the absence or in the presence of anhydrous sodium acetate, gives only one substance, the constitution of which has not been investigated, but which appears to have the empirical formula $C_{24}H_{18}O_3Br_4$.

EXPERIMENTAL.

Action of Methylmagnesium Iodide on Diphenoyl Chloride.—The solid acid chloride (9 g.; 1 mol.) was gradually added to a decanted Grignard reagent prepared from 40 g. (8 mols.) of methyl iodide. When the initial vigorous reaction was over, the mixture was boiled for 3 hours, and then decomposed in the usual manner. The semi-crystalline residue (8 g.) obtained by removal of the ether was crystallised from light petroleum (b. p. 80—100°) and so separated into a more and a less soluble fraction. The former crystallised from light petroleum (b. p. 60—80°) in rectangular prisms (2 g.), m. p. 138—139°, and was 2 : 2'-*di-α-hydroxy*iso*propyldiphenyl* (Found: C, 80·0; H, 8·0. $C_{18}H_{22}O_2$ requires C, 79·95; H, 8·2%). The less soluble fraction crystallised from acetone–light petroleum (b. p. 60—80°) in needles (2 g.), m. p. 164—165°, and was 2-*acetyl*-2'-*α-hydroxy*iso*propyldiphenyl* (Found: C, 80·1; H, 6·9. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%). Addition of benzene to the original reaction mixture, with consequent increase in the boiling temperature, had the effect of slightly increasing the proportion of glycol formed.

Action of Methylmagnesium Iodide on 2 : 2'-Diacetyldiphenyl.—Diacetyldiphenyl (12 g.; 1 mol.) was gradually added to a decanted Grignard reagent prepared from 28 g. (4 mols.) of methyl iodide. The mixture was then boiled for 3 hours and decomposed in the usual manner. Evaporation of the dried ethereal extract gave 10 g. of almost pure 2 : 2'-di-α-hydroxy*iso*propyldiphenyl, and this, crystallised from light petroleum, became 8 g. of the pure glycol. 2 : 2'-Diacetyldiphenyl was conveniently prepared by the method of Zincke and Tropp (*Annalen*, 1908, **363**, 305); it melted at 94—95° and not at 84° as these authors state.

Action of Methylmagnesium Iodide on Methyl Diphenate.—The ester (9 g.; 1 mol.) was added rapidly to a Grignard reagent made from 50 g. (10 mols.) of methyl iodide, and the mixture boiled for 3 hours. After the usual subsequent procedure, 4 g. of pure glycol were obtained.

*Action of Methylmagnesium Iodide on 2-Acetyl-2'-α-hydroxy*iso*propyldiphenyl.*—The alcohol-ketone (1 mol.) was added to 4 mols. of Grignard reagent, and the mixture boiled for 6 hours. The yield of pure glycol was 10% of the theoretical.

Formation of 2 : 2'-Di-α-methylethenyldiphenyl.—(*a*) The glycol was added to 10 parts of phosphorus tribromide and the solution was heated at 90—100° for 15 minutes, cooled, and decomposed with ice. Extraction with ether, etc., led to a solid which, when crystallised from light petroleum (b. p. 40—60°), gave the 2 : 2'-*di-α-methylethenyldiphenyl* in prisms, m. p. 97—98° (yield, 85%) (Found: C, 92·15; H, 7·8. $C_{18}H_{18}$ requires C, 92·3; H, 7·7%). Replacement of the phosphorus tribromide by a mixture of this with the pentabromide caused no change in the result of the reaction, and a mixture of the tribromide with chloroform was without action on the glycol.

(*b*) The glycol was heated at 150° in a current of dry hydrogen chloride for 6 hours. Almost pure hydrocarbon remained (Found: C, 92·15; H, 7·8%).

Bromination of 2 : 2'-Diacetyldiphenyl.—(*a*) A solution of bromine (4 atom.) in glacial acetic acid was added to one of diacetyldiphenyl (1 mol.) in the same solvent. On warming to 50—60°, decolorisation occurred, and after a further short warming the solution was cooled; crystals then separated. These were recrystallised from methyl alcohol and then from light petroleum (b. p. 80—100°), and gave hair-like needles, m. p. 134—135°, of a *substance* (Found: C, 42·8; H, 2·8; Br, 47·3. $C_{24}H_{18}O_3Br_4$ requires C, 42·8; H, 2·7; Br, 47·4%). (*b*) The process was repeated, only 90% of the proportion of bromine being used in presence of anhydrous sodium acetate. The same product was obtained.

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UNIVERSITY OF LONDON, BEDFORD COLLEGE. [*Received, November 16th, 1936.*]

25. *The Valency Angle of Bivalent Lead: The Crystal Structure of Ammonium, Rubidium, and Potassium Pentabromodiplumbites.*

By H. M. POWELL and H. S. TASKER.

COMPOUNDS of the type MB_2X_5, where M is an alkali metal or ammonium, B a bivalent metal, and X a halogen, are formed by the elements of group IVB and by mercury. The present work was begun with the object of determining the constitution of the compounds in which the bivalent element is lead. A preliminary X-ray survey of some of these substances showed that ammonium and rubidium lead bromides were most suitable for structure determination, and these compounds have been studied in detail. The corresponding potassium compound is shown to be isomorphous. The structures contain lead bromide molecules and therefore make possible a determination of the valency angle of bivalent lead.

The Structure of Ammonium Pentabromodiplumbite.—The substance was prepared by cooling an aqueous solution of the component salts in the proportions given by Wells and Johnstone (*Amer. J. Sci.*, 1893, **46**, 28). It forms tetragonal plates, tabular on (001), the plate edge being the [100] axis, and larger crystals show traces of a form (*h0l*). The crystals are optically uniaxial, have high refractive indices and show rather weak negative double refraction. The unit cell dimensions are $a = 8{\cdot}39$, $c = 14{\cdot}34$ A. These dimensions and the density determined by a pyknometer method give the number of molecules per unit cell as 3·77. The correct value should be 4 molecules per cell and the discrepancy is due to impurity of the material. The substance is obtained from very concentrated ammonium bromide solution and cannot be washed without decomposition; it therefore always contains an excess of ammonium bromide. Different samples of the material were analysed, and the same samples used for density determination. The composition was found to be variable, high nitrogen content coinciding with high bromine results. From the analyses, the amount of excess ammonium bromide was calculated, and then from the known density of ammonium bromide and the density 5·46, calculated for the compound on the assumption of 4 molecules per cell, values for the density of the mixtures were obtained consistent with the observed ones (Table I). Analysis (1) was performed on the initial small sample made to check the method of preparation, and there was insufficient material for a density determination.

TABLE I.

	Pb (as $PbCrO_4$), %.	Br (as AgBr), %.	N (as N_2), %.	Density of mixture, calc.	Density, obs. (pyknometer), 22°/4°.
(1)		48·0	1·9	—	—
(2)		49·7	2·1	5·19	5·16
(3)	49·2	50·4	2·2	5·02	5·15
(Calc.).................	49·8	48·1	1·7		

In (3) the calculation was made on the assumption that the bromine and nitrogen figures were correct, the lead value being regarded as the least reliable.

A complete series of 15° oscillation photographs from a plate 0·2 × 0·2 × 0·05 mm. about the *a* and *c* axes was taken with copper radiation. Indexed by the chart method, they showed the systematic absence of *h0l* spectra, and the absences corresponding to body-centring. Combined with the negative result of a liquid-air test for pyroelectricity, this gives the space group as *I*4/*mcm*. A complete structure based on this space group was deduced as follows.

In the cell there are 8Pb, 20Br, and $4NH_4$, which may be arranged among the possible equivalent atomic positions as

(1) 8Pb + 16Br + 4Br + $4NH_4$, (2) 8Pb + 8Br + 8Br + 4Br + $4NH_4$, (3) 8Pb + 8Br + 4Br + 4Br + 4Br + $4NH_4$, (4) 4Pb + 4Pb + 8Br + 8Br + 4Br + $4NH_4$, or (5) 4Pb + 4Pb + 16Br + 4Br + $4NH_4$. Arrangement (2) is excluded since if any two of the fourfold positions are occupied it is impossible to place the remaining atoms in three eightfold positions to give satisfactory interatomic distances. The intensities of 00*l* spectra show that the structure has a *c* axis parameter, and since the space occupied by atoms in fourfold positions in (3) and (4) makes it impossible for any other atom to enter an eightfold position with such a parameter, these two possibilities (3) and (4) are also re-

jected. In (5), 16Br would have to be in the 16-fold position with a *c* parameter, and any attempt to base a structure on this breaks down through impossible interatomic distances and incompatibility with observed intensities.

Arrangement (1) alone gives a satisfactory structure. Since three of the four 16-fold positions would require eight bromine atoms to be in one plane within an area of 8·39 × 8·39 A., which can only contain half the number, the only possible position for 16Br is $x, \frac{1}{2} + x, z$, etc. [position (*l*), " International Tables for Crystal Structure "]. When 16Br are given these co-ordinates, with x and z restricted so that no two bromines shall interpenetrate, the only dimensionally possible positions for the other atoms are at once fixed and the structure obtained has 16Br in (*l*) $x, \frac{1}{2} + x, z$, etc.; 8Pb in (*h*) $u, \frac{1}{2} + u, 0$, etc.; $4NH_4$ in (*a*) $00\frac{1}{2}$, etc., and 4Br in (*b*) 000, etc. The values found for the parameters are $x = 0{\cdot}163 \pm 0{\cdot}003$, $u = 0{\cdot}158 \pm 0{\cdot}002$, $z = 0{\cdot}363 \pm 0{\cdot}001$.

The 00*l* intensities are independent of x and u, and for these agreement is found if z or $\frac{1}{2} - z = 0{\cdot}363$ (Table II).

TABLE II.

Indices.	Intensity, calc.	Intensity, obs.	Indices.	Intensity, calc.	Intensity, obs.
002	380	vvs	$00\underline{12}$	7	m
004	15	m	$00\underline{14}$	48	s
006	180	vs	$00\underline{16}$	35	ms
008	150	vs	$00\underline{18}$	7	nil
$00\underline{10}$	9·5	m			

From contour diagrams showing the effect of simultaneous variation of x and u on the intensities of 20 spectra of the types *h*00, *hh*0, and *hk*0 which are independent of z, agreement is found with observation for $x = 0{\cdot}163$, $u = 0{\cdot}158$, or for the symmetrically related values of x and u (Table III).

TABLE III.

Indices.	*I*, calc.	*I*, obs.	Indices.	*I*, calc.	*I*, obs.	Indices.	*I*, calc.	*I*, obs.
200	52	s	440	27	nil (ms)	640	11	m
400	83	s	550	0	nil (nil)	370	29	ms
600	106	vs	660	46	m (s)	820	2	vw
800	0·2	nil	310	119	vs	570	0·7	nil
$\underline{10}00$	56	m	420	31	m	910	16	m
$\bar{1}10$	21	mw (mw)	350	14	m	840	2·7	w
220	36	m (s)	620	5	mw	930	34	s
330	120	s (vs)	710	3·7	vvw	950	16	mw

In general, the observed intensities in the series *hh*0 are weaker than the calculated, but this is caused by the large absorption due to the crystal shape. Intensities obtained with a large crystal on which a face had been ground nearly parallel to (110) are given in parentheses above. The correct combination of the alternative values of parameters is obtained from *hkl* spectra. The intensities of these and others of type *h*0*l* are shown in Table IV.

TABLE IV.

Indices.	*I*, calc.	*I*, obs.	Indices.	*I*, calc.	*I*, obs.	Indices.	*I*, calc.	*I*, obs.
112	1·5	nil	143	60	s	$12\underline{11}$	32	ms
211	30	m	404	0	nil	$6\bar{0}6$	33	ms
114	3·5	w	127	1·3	nil	$40\overline{\underline{10}}$	0·5	nil
123	178	vs	136	56	s	$11\overline{\underline{12}}$	0	nil
202	4·5	mw	145	30	s	$20\overline{\underline{12}}$	0	nil
222	12	m	208	7·6	m	$6\bar{0}8$	45	ms
204	4	nil	523	56	s	$40\overline{\underline{12}}$	0·3	nil
132	33	ms	129	14	m	$60\overline{\underline{10}}$	4·7	w
125	67	s	352	3·2	m	$20\overline{\underline{14}}$	4·1	w
116	2·8	vw	525	34	ms	$40\overline{\underline{14}}$	11·3	m
323	5·6	vw	$11\underline{10}$	0	nil	$42\overline{\underline{14}}$	3	w
206	8·2	m	$60\bar{2}$	15·5	m	$60\overline{\underline{12}}$	10·2	w
402	9·4	w	408	14·3	m	$\underline{10}0\bar{2}$	11·4	mw
332	25	ms	604	3·9	vw	$\bar{6}0\underline{14}$	68	s
422	6·3	mw	$20\underline{10}$	0	nil			

All intensities were calculated by the formula

$$I \propto \frac{1 + \cos^2 2\theta}{\sin 2\theta} \cdot |S|^2$$

and corrected when necessary for position of the spot on the layer line. Observed intensities were estimated visually with the aid of a graduated scale.

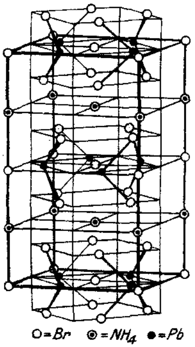
Rubidium Pentabromodiplumbite.—A small quantity of this substance was prepared by the method of Wells and Johnstone (*loc. cit.*). It forms tetragonal crystals which have rather weak negative double refraction. The oscillation photographs of these crystals taken with copper radiation are almost superposable on the photographs from the ammonium compound taken over corresponding ranges of oscillation. They give for the cell dimensions $a = 8{\cdot}41$, $c = 14{\cdot}5$ A., and a density, calculated for 4 molecules per unit cell, 5·76. The space group is $I\ 4/mcm$ and the atomic positions are the same as those for ammonium pentabromodiplumbite with rubidium replacing ammonium. Good agreement between observed and calculated intensities is obtained with 4Rb in (*a*) $00\tfrac{1}{4}$, etc.; 4Br in (*b*) 000, etc.; 8Pb in (*h*) $u, \tfrac{1}{2} + u, 0$, etc.; $u = 0{\cdot}158$; and 16Br in (*l*) $x, \tfrac{1}{2} + x, z$, etc., $x = 0{\cdot}163$, $z = 0{\cdot}365$ (Table V). The effect of substitution of rubidium for ammonium is shown especially in the $00l$ spectra which may be compared with the corresponding spectra in Table II.

TABLE V.

Indices.	I, calc.	I, obs.	Indices.	I, calc.	I, obs.	Indices.	I, calc.	I, obs.
002	280	vs	116	3·4	m	288	5·6	m
004	54	s	125	76·5	vs	279	1·5	m
006	117	s	127	1·5	vw	27$\underline{11}$	23	s
008	190	vs	129	11	m	25$\underline{11}$	17·2	s
00$\underline{10}$	6·7	w	12$\underline{11}$	34	s	26$\underline{10}$	0	nil
00$\underline{12}$	10	m	22$\underline{10}$	0	nil	228	15·2	s
00$\underline{14}$	31	ms	14$\underline{11}$	19·4	s	24$\underline{12}$	3·3	w
00$\underline{16}$	50	ms	24$\underline{10}$	0·5	nil	26$\underline{12}$	0·9	nil
00$\underline{18}$	4	nil	198	34	ms			

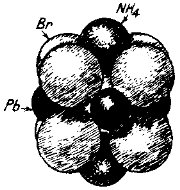
Potassium Pentabromodiplumbite.—A quantity of this substance was prepared according to the directions of Wells (*Amer. J. Sci.*, 1893, **45**, 121). It forms tetragonal plates with the

FIG. 1.



Unit cell showing each lead atom linked to two bromines.

FIG. 2.



The packing of the atoms shown by use of ionic radii; the lead–bromine links by the interpenetration of the spheres.

[110] axis as plate edge. From oscillation photographs with copper radiation the unit cell dimensions were found to be $a = 8{\cdot}14$, $c = 14{\cdot}1$ A. The photographs are nearly superposable on the corresponding ones of the ammonium compound and the structure is clearly similar to that of the previous compounds.

Discussion of the Structure.—A complete unit cell is illustrated in Fig. 1, and the centre portion is further illustrated in Fig. 2, which is drawn to the same scale and shows the

essential character of the structure. It consists of vertical rows of alternate bromine and alkali (or ammonium) ions with lead bromide molecules arranged in groups of four around these rows. A list of near neighbours of the various atoms is given in Table VI.

TABLE VI.

	$NH_4Pb_2Br_5$.		$RbPb_2Br_5$.	
	Neighbours.	Distance, A.	Neighbours.	Distance, A.
Pb	$2Br_{II}$	2·89 ±0·05	$2Br_{II}$	2·89
	$2Br_I$	3·16 ±0·02	$2Br_I$	3·17
	$4Br_{II}$	3·35 ±0·05	$4Br_{II}$	3·39
	1Pb	3·74 ±0·05	1Pb	3·76
Br_I (at 000)	4Pb	3·16	4Pb	3·17
	$2NH_4$	3·59	2Rb	3·62
	$8Br_{II}$	3·70	$8Br_{II}$	3·71
Br_{II} at $(x, \frac{1}{2}+x, z)$	1Pb	2·89	1Pb	2·89
	2Pb	3·35	2Pb	3·39
	$2NH_4$	3·59	2Rb	3·56
	$2Br_I$	3·70	$2Br_I$	3·71
	$1Br_{II}$	3·93	$1Br_{II}$	3·91
NH_4 or Rb	$2Br_I$	3·59	$2Br_I$	3·62
	$8Br_{II}$	3·59	$8Br_{II}$	3·56

The ammonium or alkali-metal ion has for neighbours two bromine ions and eight bromines which are linked to lead. This co-ordination is similar to that found in the compound $Cs_3[CoCl_4]Cl$ (Powell and Wells, J., 1935, 359), where one of the cæsium ions has ten chlorine neighbours consisting of two chlorine ions and eight chlorines which are linked to cobalt. The distance between the positive and negative ions is in all cases slightly greater than it would be in the corresponding alkali (or ammonium) halide crystallising in an 8-co-ordination CsCl type of structure, but the distance of the positive ion from the other eight halogens does not obey a similar rule.

The bromine ions show a remarkable co-ordination, having no less than 14 other atoms in contact with them. This type of co-ordination, which may be seen in Fig 2, is made possible by the favourable ratios of the radii of the atoms involved. To obtain this arrangement the central bromine ion may first be regarded as at the centre of a cube in contact with 8 bromines at the corners. The cube is then flattened so that the 8 bromines, which originally are not touching, come into contact in four pairs. This leaves two spaces, at the centres of the upper and lower faces of the cube, large enough for the entry of ammonium ions into contact with the central bromine ion. When allowance is made for the shortening of the distances of each lead to two of its bromine neighbours the four smaller spaces on the sides of the flattened cube permit the approach of four lead atoms into contact with the central bromine.

Each lead has two close bromine neighbours at 2·89 ± 0·05 A. This distance is less than the sum of the ionic radii (3·16, Pauling; or 3·28, Goldschmidt). It is also considerably less than the distance to the next set of neighbours at 3·16 A., which are two bromine ions of the vertical rows. The next four bromine neighbours at 3·35 A. are all closely attached to other lead atoms. A probable lead-to-bromine distance for a covalent link may be deduced from the mercury–bromine distance obtained from electron diffraction experiments with mercuric bromide vapour. Braune and Knoke (*Z. physikal. Chem.*, *B*, 1933, **23**, **163**) give for this 2·40, and G. I. Jenkins (private communication) 2·44 A. From the latter value by addition of the difference of the atomic radii of lead and mercury the value 2·63 A. is obtained as a probable lead–bromine covalent distance. Whether our higher observed value corresponds to a covalent link or something intermediate between this and an ionic linkage, we may regard the structure as containing lead bromide molecules, since this accords best with the general characteristics of the structure. Thus the two nearest bromine neighbours of the lead atoms are much closer than the two which are known certainly to be ionised; and in agreement with this view there are few positive neighbours of the linked bromine atoms and no marked tendency for the lead atoms to keep widely apart.

The two bonds of the lead bromide molecule will be formed by the $6(p)^2$ electrons of the

lead atom, and according to the wave-mechanics treatment of the chemical bond by Pauling (*J. Amer. Chem. Soc.*, 1931, **53**, 1367), the angle between these bonds should be near to 90°. From the parameters found, the angle subtended at the centre of the lead by the two nearest bromine atoms is calculated to be $85\frac{1}{2}° \pm 2°$, a value in agreement with the prediction and providing confirmation of the essentially covalent character of the links. The bent form of the molecule is in contrast with the linear configurations found for the dimethylthallium ion (Powell and Crowfoot, *Z. Krist.*, 1934, **87**, 370) and the mercuric chloride molecule (Braekken, *ibid.*, **89**, 448), in both of which covalencies are formed by the $6(s)^2$ electrons.

Department of Mineralogy, University Museum, Oxford. [*Received, August 12th, 1936.*]

26. *The Application of Ullmann's Reaction to the Preparation of Dinaphthyls.*

By Herbert H. Hodgson and Reginald L. Elliott.

Chudožilov (*Chem. Listy*, 1925, **19**, 187) applied Ullmann's method (*Ber.*, 1901, **34**, 2174; *Annalen*, 1904, **332**, 38) of heating aromatic halogeno-compounds with finely divided copper to form diaryls to the iodonitronaphthalenes, and reported that only the homonuclear derivatives afforded dinaphthyls. Further, from a study of the 1-iodo-2-, -3-, and -4-nitronaphthalenes and of 2-iodo-1-nitronaphthalene, Chudožilov concluded that the iodine should preferentially be in the ortho-position to the nitro-group for satisfactory results. Cumming and Howie (J., 1931, 3176) supported Chudožilov's generalisations after an investigation of substituted tetrahydronaphthalenes. The effect of the unsubstituted nucleus on the iodine atom and its configuration with respect to the nitro-group appears, however, to have been overlooked, and the present investigation has established the very considerable influence of the adjacent nucleus.

Dinaphthyl formation by Ullmann's method appears to depend on the ability of the copper to form covalent cuprous iodide with the substituted iodine, since sodium has been found by Cumming and Howie (*loc. cit.*) not to effect condensation even in the case of the ortho-compounds. This reaction thus differs from the Fittig mechanism in that copper does not release one of its electrons to the carbon and so enable ionic iodine to separate, as sodium would do whether acting as metal or in sodium alkoxide, and consequently radical formation will depend upon the ease of detachment of neutral iodine from neutral carbon as depicted: $2RI + 2Cu \longrightarrow 2R^{\cdot} + Cu_2I_2 \longrightarrow R{:}R + Cu_2I_2$. Now the unsubstituted nucleus has been found to exert a restraining (electron-attracting) influence in numerous naphthalene derivatives, the most familiar example, perhaps, being the fact that β-naphthylamine is a stronger base than its α-isomeride; the easier detachment of iodine from 3-iodo-1-nitronaphthalene than from 1-iodo-3-nitronaphthalene (cf. Chudožilov; Cumming and Howie, *locc. cit.*) provides additional evidence of this kationoid effect. Consequently Chudožilov's ortho-generalisation must be modified by taking into account the effect of the unsubstituted nucleus, which will depend on the position of the iodine. A test case for this effect would appear to be furnished by the fact that in a relatively inert medium such as nitrobenzene, the 4-iodine (*i.e.*, meta to the nitro-group) was removed by copper from 1 : *4-di-iodo-2-nitronaphthalene* instead of the 1-iodine as would be expected from Chudožilov's generalisation, with the formation of 4 : 4′-*di-iodo*-3 : 3′-*dinitro*-1 : 1′-*dinaphthyl*. The constitution of the last-named product was established by the production from it on heating of 3 : 3′-dinitro-1 : 1′-dinaphthyl and iodine.

The more severe operation of the dry heating of copper with 1 : 4-di-iodo-2-nitronaphthalene resulted mainly in the formation of 1-iodo-3-nitronaphthalene, though a little 1-iodo-2-nitronaphthalene was detected; the production and preservation of both the previous compounds in such drastic reactions testify to the strength of the bond between the iodine and the α-carbon atom, *i.e.*, to the restraining effect of the adjacent nucleus. With 1 : 2-di-iodo-4-nitronaphthalene, only α-nitronaphthalene could be isolated from the Ullmann reaction product, owing probably to the accommodation of the 2-iodine in

relieving the strain on the 1-iodine, and thereby promoting ultimately the hydrogenation of both positions in the destructive decomposition which arises.

Cumming and Howie (*loc. cit.*) have reported the preparation of 3 : 3'-dinitro-2 : 2'-dinaphthyl in microscopic yield by the oxidation with bromine of the 3 : 3'-dinitro-2 : 2'-bistetrahydronaphthyl obtained from Ullmann's reaction with 2-iodo-3-nitrotetrahydronaphthalene. The present authors, however, could only obtain 2-nitronaphthalene when the reaction was applied to 3-iodo-2-nitronaphthalene itself, with no indication of dinaphthyl formation, a result entirely in harmony with the recorded instability of the 2 : 3-halogenonitronaphthalenes (Hodgson and Elliott, J., 1936, 1151), and in contradiction to Chudožilov's ortho-generalisation.

In marked contrast to 3-iodo-2-nitronaphthalene, which is non-volatile in steam, 3-iodo-1-nitro- and 1-iodo-3-nitro-naphthalene are volatile to the extent of 0·35 g. and 0·08 g., respectively, per litre of distillate.

Experimental.

Preparation of 4 : 4'-*Dinitro*-2 : 2'-*dinaphthyl*.—3-Iodo-1-nitronaphthalene (4 g.) (Hodgson and Elliott, J., 1934, 1706) was intimately mixed with precipitated copper powder (7 g.), and refluxed for 5 hours with freshly distilled and carefully dried nitrobenzene (25 c.c.); the liquid was filtered hot, 10 c.c. of nitrobenzene were removed by distillation, and the remainder was kept for 36 hours; deep brown, lustrous plates of 4 : 4'-*dinitro*-2 : 2'-*dinaphthyl* (0·2 g.) separated, m. p. 316° after recrystallisation from nitrobenzene (Found : N, 8·3. $C_{20}H_{12}O_4N_2$ requires N, 8·1%). After removal of the nitrobenzene from the mother-liquor by steam distillation and extraction of the residue with boiling glacial acetic acid, 1·75 g. of unchanged 3-iodo-1-nitronaphthalene were obtained. The residue from the first filtration (above), consisting mainly of copper powder and cuprous iodide, was extracted with boiling nitrobenzene, a further 0·15 g. of crude (m. p. 306°) 4 : 4'-dinitro-2 : 2'-dinaphthyl being obtained; total yield, 31·5%. Prolonged refluxing, for periods up to 10 hours, removed the iodine, but the product was mainly tar and the yields of the dinaphthyl were decreased.

Ullmann's Reaction with 2-Iodo-3-nitronaphthalene.—Copper powder (3 g.) and 2-iodo-3-nitronaphthalene (2 g.) (Hodgson and Elliott, *loc. cit.*) were refluxed for 5 hours with nitrobenzene (20 c.c.), this was then removed from the hot filtered liquid by steam distillation, and the residue was extracted with boiling glacial acetic acid. From this extract, only β-nitronaphthalene (0·3 g., m. p. 79°) could be obtained; the steam distillate afforded a further 0·08 g. No product of higher m. p. indicative of dinaphthyl formation could be identified in the copper residues.

Preparation of 1 : 4-*Di-iodo-2-nitronaphthalene*.—4-Iodo-2-nitronaphthylamine (20 g.) (Hodgson and Elliott, J., 1935, 1850), suspended in glacial acetic acid, was slowly added to a solution of sodium nitrite (6 g.) in concentrated sulphuric acid (100 c.c.) kept below 20°. The excess of nitrous acid was destroyed by urea, and the diazo-solution added rapidly to a saturated aqueous solution of potassium iodide (300 c.c.) at 15°, the temperature being allowed to reach 75°; much iodine and hydrogen iodide were evolved. After 1 hour, the mixture was stirred into cold water (1 l.); the precipitated 1 : 4-*di-iodo-2-nitronaphthalene* was extracted repeatedly with 10% aqueous potassium iodide (500 c.c.) and then with 90% alcohol (300 c.c.) to remove iodine; it was finally recrystallised three times from glacial acetic acid and obtained in dark brown scales, m. p. 126° (Found : I, 59·5. $C_{10}H_5O_2NI_2$ requires I, 59·8%).

1 : 2-*Di-iodo-4-nitronaphthalene*, obtained from 2-iodo-4-nitro-1-naphthylamine (Hodgson and Elliott, J., 1934, 1705) in like manner, crystallised from glacial acetic acid in deep chocolate-brown needles, m. p. 172° (Found : I, 59·6. $C_{10}H_5O_2NI_2$ requires I, 59·8%).

4 : 4'-*Di-iodo*-3 : 3'-*dinitro*-1 : 1'-*dinaphthyl*.—1 : 4-Di-iodo-2-nitronaphthalene (2 g.) and copper powder (2 g.) were refluxed for 5 hours with nitrobenzene (25 c.c.), and the residue remaining after steam distillation was extracted with boiling glacial acetic acid. After 24 hours, 4 : 4'-*di-iodo*-3 : 3'-*dinitro*-1 : 1'-*dinaphthyl* separated as a light brown, micro-crystalline powder, which softened with apparent decomposition at 220° and sublimation of iodine, fused at 275—280°, and decomposed completely at 375° (Found : I, 42·3. $C_{20}H_{10}O_4N_2I_2$ requires I, 42·6%). A larger amount, heated slowly above 220°, lost iodine and became 3 : 3'-dinitro-1 : 1'-dinaphthyl, the residue on crystallisation from glacial acetic acid affording golden-yellow plates of this compound, m. p. 281° (Cumming and Howie, *loc. cit.*, give m. p. 281°) (Found : N, 8·2. Calc. for $C_{20}H_{12}O_4N_2$: N, 8·1%). The acetic acid mother-liquor above, from which the 4 : 4'-di-iodo-3 : 3'-dinitro-1 : 1'-dinaphthyl had crystallised, was poured into water; 1-iodo-2-nitronaphtha-

lene was precipitated (0·15 g.) and after two crystallisations from glacial acetic acid it had m. p. and mixed m. p. with an authentic specimen (Hodgson and Kilner, J., 1926, 9) 111° (Found : I, 42·1. Calc. for $C_{10}H_6O_2NI$: I, 42·4%).

Action of Copper Powder alone on 1 : 4-*Di-iodo-2-nitronaphthalene*.—During the dry fusion of 1 : 4-di-iodo-2-nitronaphthalene (2 g.) with precipitated copper powder (2 g.), no reaction took place below 180—190°, but a glacial acetic acid extract of the reaction product after 2 hours' heating at 180—210°, when poured into water, afforded a brick-red precipitate (m. p. 112°) which, recrystallised once from glacial acetic acid and once from alcohol, gave orange-yellow needles (0·3 g.) of 1-iodo-3-nitronaphthalene, m. p. and mixed m. p. with an authentic specimen, 147° (Found : I, 42·3. Calc. for $C_{10}H_6O_2NI$: I, 42·4%). A trace of 1-iodo-2-nitronaphthalene (0·05 g.) was also identified (m. p. and mixed m. p.) in the acetic acid extract.

Action of Copper on 1 : 2-*Di-iodo-4-naphthalene*.—After 5 hours' refluxing with nitrobenzene and the procedure described above for the isomeride, this substance was recovered unchanged, but the iodine was completely removed after 10 hours' boiling, with formation of much tar, from which only α-nitronaphthalene could be extracted. Dry fusion, as above, produced complete decomposition at 200°.

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TECHNICAL COLLEGE, HUDDERSFIELD. [*Received, November 24th*, 1936.]

27. *The Rotatory Dispersion of Organic Compounds. The First Oxidation Product of Ascorbic Acid.*

By W. C. G. BALDWIN.

THIS paper contains an account of work carried out at the suggestion of the late Prof. T. M. Lowry, F.R.S., to whom the author was greatly indebted.

It has been shown (Herbert, Hirst, Percival, Reynolds, and Smith, J., 1933, 1270, etc.) that ascorbic acid is reversibly oxidised by agents such as aqueous iodine to a lactone (2 : 3-diketogulonolactone), which in aqueous solution gradually changes into the corresponding acid. Some data on the mutarotation, absorption spectra, and rotatory power of such solutions were also given, and, together with measurements on the parent acid (Lowry and Pearman, J., 1933, 1444; Herbert, Hirst, and Wood, J., 1933, 1564), have been of service in elucidating the problems connected with this reactive substance. However, important deficiencies in these series of data are analyses of: (*a*) the rotatory dispersion of the aqueous lactone, and of the salt of the hydrated lactone; (*b*) mutarotation of the lactone in water. These are now supplied.

(a) *Rotatory Dispersion of the Lactone*.—This substance dissolved in water gives perfectly simple dispersion over the range 6708—3350 A. (see Table I). The wave-length from the Drude equation, 2152 A., is in good agreement with the value expected from examination of the absorption curve published by Herbert *et al.* (*loc. cit.*). The major contribution to the activity therefore finds its origin in the induced dissymmetry of the -CO-O- group under the influence of the asymmetry of the molecule.

Rotatory dispersion of the sodium salt. This compound has been shown to possess two absorption bands, at 2450 and 2950 A. (*loc. cit.*). Investigation over a limited range shows the probability of the inactivity of the low-frequency band (cf. Lowry, J., 1933, 1448). The rotatory dispersion of this salt is centred at 2316 A., in fair agreement with the value for the second absorption band (see Table II). Other cases of this inactivity of absorption bands are not unknown, but rather uncommon, the most striking example being afforded by the nicotinium ion.

(b) *Mutarotation of the Lactone*.—Solutions of this substance underwent mutarotation according to a unimolecular law, the course of the reaction being followed polarimetrically. Different preparations did not give quite reproducible values for the velocity constant, but a typical series of readings is appended (Table III).

A preliminary series for more dilute and acid solutions, previously given (*loc. cit.*), quoted negative final values for rotations, but in using concentrated solutions the trans-

TABLE I.

Rotatory Dispersion of the Lactone in Water at 20°.

c = 4·760 g. of lactone per 100 c.c.; l = 2 dm.
$[\alpha] = 12{\cdot}242/(\lambda^2 - 0{\cdot}04630)$; λ_0 = 2152 A.

(Values corrected for slight initial errors, and for mutarotation effects.)

λ.	[α], obs.	[α], calc.	Diff.	λ.	[α], obs.	[α], calc.	Diff	λ.	[α], obs.	[α], calc.	Diff.
6708	31·2°	30·4°	−0·8°	5209	54·1°	54·5°	0·4°	3944	112·0°	112·0°	0·0°
6438	33·2	33·3	0·1	5153	55·9	56·0	0·1	3925	110·7	113·9	3·2
6362	34·5	34·2	−0·3	5086	57·8	57·8	0·0	3822	122·8	122·7	−0·1
6104	37·6	37·6	0·0	4800	66·5	66·5	0·0	3665	139·0	139·0	0·0
5893	41·1	40·8	−0·3	4602	73·5	74·2	0·7	3536	155·0	155·5	0·5
5782	42·6	42·6	0·0	4358	86·5	85·5	−1·0	3498	162·4	162·0	−0·4
5780	42·6	42·6	0·0	4290	89·8	89·0	−0·8	3490*	162·1	162·1	0·0
5700	44·0	44·0	0·0	4202	92·2	93·9	1·7	3356*	190·0	184·5	−5·5
5468	48·1	48·6	0·5	4130	98·5	98·5	0·0	3353*	192·0	185·0	−7·0
5461	48·6	48·6	0·0	4000	107·5	107·8	0·3				

* l = 1 cm.

TABLE II.

Rotatory Dispersion of the Sodium Salt in Water at 20°.

c = 3·879 g. of salt in 100 c.c.
$[\alpha] = -5{\cdot}96/(\lambda^2 - 0{\cdot}0536)$; λ_0 = 2316 A.

λ.	[α], obs.	[α], corr.	λ.	[α], obs.	[α], corr.	λ.	[α], obs.	[α], corr.
6708	−13·40	−14·99°	5780	−19·10°	−21·35°	5209	−24·48°	−27·38°
6438	−14·70	−16·42	5700	−19·70	−22·00	5153	−25·26	−28·20
6104	−16·78	−18·74	5468	−21·65	−24·20	5105	−25·90	−28·95
5893	−18·18	−20·30	5461	−21·52	−24·05	5086	−26·02	−29·10
5782	−18·80	−21·00	5219	−24·10	−26·92			

TABLE III.

Mutarotation of 2 : 3-Diketogulonolactone in Water at 20°.

λ = 5461 A.; c = 4·76 g. of lactone per 100 c.c.; α_0 = 4·62°; α_{166} = −0·01°.
$k(\text{hr.}^{-1}) = (2{\cdot}303/t) . \log (\alpha_0 - \alpha_\infty)/(\alpha_t - \alpha_\infty)$; mean k = 0·0247 hr.$^{-1}$.

Reading.	t, hrs.	α_t.	k.	Reading.	t, hrs.	α_t.	k.	Reading.	t, hrs.	α_t.	k.
1	0·20	4·59°	0·0242	8	2·70	4·28°	0·0282	15	53·0	1·48°	0·0214
2	0·25	4·60	0·0156	9	3·58	4·17	0·0283	16	70·0	1·02	0·0216
3	0·32	4·58	0·0238	10	23·25	2·72	0·0227	17	118·0	0·35	0·0216
4	0·77	4·52	0·0269	11	27·5	2·47	0·0227	18	125·0	0·28	0·0222
5	0·85	4·46	0·0393	12	29·5	2·38	0·0224	19	142·0	0·11	0·0257
6	1·37	4·45	0·0270	13	46·7	1·71	0·0212	20	149·0	0·07	0·0275
7	1·97	4·35	0·0296	14	50·0	1·58	0·0214				

$k(\text{hr.}^{-1}) = [2{\cdot}303/(t_2 - t_1)] \log (\alpha_1 - \alpha_\infty)/(\alpha_2 - \alpha_\infty)$; mean k = 0·0216 hr.$^{-1}$.

Readings	1 & 11	2 & 12	3 & 13	4 & 14	5 & 15	6 & 16
k	0·0226	0·0224	0·0212	0·0212	0·0211	0·0213

parency was so poor after 150 hrs. that the measurements had to be abandoned, the rotation then being − 0·01°. For the same reason, the rotatory dispersion of the muta-rotated solution could not be investigated.

EXPERIMENTAL.

Preparation of Solutions of the Lactone.—Sodium hypochlorite (2*N*) was diluted slightly, and the amount of excess caustic alkali determined. Sufficient acid was then added to neutralise this, giving a solution of sodium chloride and hypochlorite only. Such mixtures evolved gas, and progressively decreased in titre, so iodometric estimation was necessary before use.

About 1 g. of very pure ascorbic acid, weighed into a 25 c.c. flask, was dissolved in water, and the calculated amount of oxidising agent run in dropwise and with efficient cooling. Measurements were then begun as soon as possible.

Absorption measurements, giving $\epsilon_{max.}$ = 400, showed that, when such concentrated solutions were used, some 4% of ascorbic acid remained unchanged, even when slight excess of hypochlorite was taken. The measurements of rotatory power should therefore be corrected to the

higher figure given by Herbert *et al.* (*loc. cit.*) for dilute solutions through multiplication by a small factor. It should be pointed out, however, that the best value obtained, $[\alpha]_{5780} = 44 \cdot 8°$, was for a neutral 4% solution, whereas that of Herbert *et al.* was 46·8° for < 1% acid solution of lactone. The value given by them should be converted through multiplication by the M.W. factor 176/210·1, since the concentration was expressed as acid.

Readings of mutarotation and dispersion were taken on the same solution by reading the mercury yellow and green lines directly before or after any other line. Appropriate corrections for mutarotation were applied, and the resulting table shows $[\alpha]_{\lambda}^{20°}$ for t_0 in each case. Frequent checks of the accuracy of the time corrections were obtained by reading 10 duplicate lines at intervals.

Sodium Salt of the Keto-acid.—Two methods of oxidation were tried with similar results, and slight corrections had to be applied as before. After the oxidation, the necessary quantity of sodium carbonate or bicarbonate was added, but in every case it was impossible to produce a solution of sufficient concentration transparent to rays shorter than about 5086 A. for 2 dm.

SUMMARY.

(*a*) The rotatory dispersion of 2 : 3-diketogulonolactone is simple, with $\lambda_0 = 2152$ A.

(*b*) The rotatory dispersion of the corresponding sodium salt is also simple, with $\lambda_0 =$ 2316 A. The first absorption band is probably inactive.

(*c*) The mutarotation of the lactone in water is analysed.

(*d*) It is shown that, in 4% solution, ascorbic acid needs an excess of oxidising agent for conversion into the lactone.

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28. *Preparation and Properties of Methyldideuteramine.*

By H. J. EMELÉUS and H. V. A. BRISCOE.

WHEN soluble compounds containing the amino- or imino-group are mixed with water containing deuterium oxide there is an interchange, resulting in partial substitution of deuterium for hydrogen in the amine groups. Quantitative measurements in these laboratories (unpublished : private communication) have shown that equilibrium is set up rapidly, and that in the case of methylamine hydrochloride the available deuterium distributes itself evenly between the two hydrogen atoms of the water and three out of six of the hydrogen atoms in the salt molecule. The repeated treatment of this with successive quantities of pure deuterium oxide must therefore lead to the formation of substantially pure methyldideuteramine deuterochloride ($CH_3 \cdot ND_2$,DCl), from which the corresponding amine may be liberated.

EXPERIMENTAL.

The apparatus used in carrying out this transformation is shown in the figure. The tube *A* containing a quantity of 99·5% pure deuterium oxide sealed in a vacuum was opened by the vacuum capillary opener *S*, and its contents distilled into *C*. Methylamine hydrochloride (0·6 g.) which had been recrystallised from absolute alcohol was introduced into *E*, which was attached to the apparatus by a ground joint. Quantities of 0·65, 0·73, 0·70, 0·68, and 0·55 c.c. of deuterium oxide were then measured out in turn in the graduated tube *B*, and distilled into the methylamine hydrochloride by cooling *E* in liquid air. This deuterium oxide was in each case allowed to melt in *E* with the tap *T* closed, and was warmed at 30—35° for 30 minutes, after which the residual heavy water, which had become diluted with ordinary water liberated in the interchange, was distilled back into *D*.

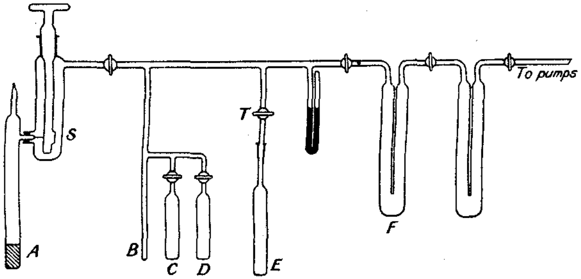
Calculation shows that, the deuterium oxide being assumed to be 99·5% pure, the above treatment should suffice for the replacement of 99·2% of the replaceable hydrogen in the methylamine hydrochloride used. After admission of dry air into *E*, excess of freshly ignited lime was introduced, and the mixture of lime and amine hydrochloride was heated at

150—200° in a vacuum. The amine evolved was collected over lime in the U-tube *F*, which was cooled in liquid air, dried by prolonged contact with lime, and then transferred to the vacuum fractionation apparatus, in which mercury valves were used in place of taps (Stock, *Ber.*, **1917**, **50**, 989).

In order to remove any trace of ammonia which might be present, the amine was distilled in a vacuum from a bath at − 90° (which retains traces of water, carbon dioxide, and less volatile impurities) to two condensers, maintained severally at − 110° to − 115° and at − 190°. The amine condensed almost quantitatively in the former, ammonia and any other similarly volatile impurities passing over to the latter.

This process was repeated, and the middle fraction further fractionated by distillation into two main fractions. These fractions and the original main fraction gave vapour-pressure curves which were identical over the whole range from − 60° to − 10°, and afforded strong evidence, therefore, that all these fractions were pure methyldideuteramine.

Measurement of Vapour Pressure.—This was carried out in accordance with the well-known method of Stock (*loc. cit.*) in an appendage to the vacuum apparatus (isolated at will by a mercury valve), consisting of a thin-walled quill tube connected with a mercury manometer of about 10 mm. bore mounted on a glass mirror scale, which could be read to 0·2 mm. or less. Temperatures were measured by means of two vapour-pressure thermometers containing severally ammonia (− 60° to − 40°) and sulphur dioxide (− 50° to − 10°).



In making a measurement, the methylamine container and the bulb of the vapour-pressure thermometer were fixed side by side and then cooled by bringing up around them a bath of about 2 l. of acetone–carbon dioxide mixture contained in a large Dewar vessel, and previously brought to approximately the desired temperature and thoroughly stirred. The mercury gauges were then read until the pressures reached minimum values, which gave a direct comparison of the absolute vapour pressures of the amine and the ammonia or sulphur dioxide at the same temperature. The temperature was then deduced from standard values of vapour pressure for the thermometric liquids.

For the purposes of comparison, a sample of pure methylamine was prepared from hydrochloride which had been thrice recrystallised from alcohol. This was distilled twice with fractional condensation, and finally fractionally distilled from a bath at − 78° and separated into three main fractions. These gave identical vapour-pressure curves, whence it is inferred that the material was homogeneous and presumably pure.

In the temperature range − 10° to − 65°, 34 readings were taken of the vapour pressure of methyldideuteramine and 38 readings from methylamine. Sufficient of these data are given in Table I to enable curves to be plotted.

The vapour pressures of methyldideuteramine are consistently less than those of methylamine by an amount which varies from 5·4 mm. at − 60° to 31·8 mm. at − 10°, but these substances could be separated only by an extremely tedious process of fractionation at low temperatures.

The b. p.'s of methylamine and its *N*-dideutero-derivative read from the log p–$1/T$ graph were − 6·1° and − 5·1° respectively. Extrapolation of the vapour-pressure curves gave values of − 6·2° ± 0·1° and − 5·2° ± 0·1° respectively. The value for methylamine is higher than that, − 6·60°, recorded by Felsing and Thomas (*Ind. Eng. Chem.*, **1929**, **21**, 1269).

TABLE I.

Temp.	V. p., NH_2Me, mm.	Temp.	V. p., ND_2Me, mm.	Temp.	V. p., NH_2Me, mm.	Temp.	V. p., ND_2Me, mm.
− 9·8°	644·7	−10·75°	588·2	−30·45°	224·7	−29·2°	225·9
−13·8	536·6	−12·9	530·4	−36·4	158·2	−35·15	158·7
−16·0	480·1	−17·4	425·3	−42·9	105·7	−41·2	109·0
−21·05	373·2	−19·8	376·2	−47·0	80·8	−48·8	65·5
−24·4	312·9	−23·25	312·8	−50·4	64·0	−50·3	59·0
				−57·6	38·3	−60·5	27·7

A comparison of the vapour pressures read from smoothed curves based on these observations is given in Table II.

TABLE II.

Temp.	−60°	−50°	−40°	−35°	−30°	−25°	−20°	−15°	−10°
V. p. of NH_2Me, mm.	31·6	66·0	127·5	174·0	231·2	304·0	392·2	505·0	640·8
V. p. of ND_2Me, mm.	26·2	60·4	118·0	161·4	216·0	283·8	371·2	480·0	609·0
Diff., mm.	5·4	5·6	9·5	12·6	15·2	20·2	21·0	25·0	31·8

The m. p.'s of the two compounds were determined by a series of direct observations of the melting of small samples condensed in a thin-walled quill tube attached to the vacuum apparatus. A stirred 2-litre alcohol–ether bath cooled by means of liquid nitrogen was used, and the melting temperature was observed with the bulb of a carbon dioxide vapour-pressure thermometer in close proximity to the sample. The beginning and end of melting could be sharply observed, and the whole transition from white opaque solid to clear liquid took place within a range of about 0·2°. The average melting temperature is therefore definite within ± 0·1°. The m. p.'s of methylamine and methyldideuteramine thus found were − 93·1° and − 89·2°, respectively.

The differences in physical properties between the two compounds are comparable with those observed for a number of other corresponding hydrogen and deuterium compounds. The purity of the specimen used was naturally limited by that of the deuterium oxide available (*viz.*, 99·5%), but it seems doubtful whether amine prepared with 100% pure deuterium oxide would give data sensibly different from those here recorded.

Absorption Spectrum of Methyldideuteramine.—The absorption spectrum was photographed on a Hilger small quartz spectrograph (E. 4), a quartz absorption cell, 10 cm. long, and Ilford Q plates being used. The light source was a hydrogen discharge tube (5000 v., 0·15 amp.), and copper and iron arc comparison spectra were superposed on the absorption spectra. The positions of the centres of the bands were measured on large-scale enlargements of the original negatives, the arc lines being used for reference standards. The error of measurement does not exceed ± 2 A. and in many cases is believed to be less than ± 1 A.

Table III contains measurements of the principal bands of methyldideuteramine. Those of methylamine have already been described (Emeléus and Jolley, J., 1935, 1612; Henri and Lasareff, *J. Chim. physique*, **1935**, **32**, 353).

TABLE III.

λ (A.).	ν (cm.⁻¹).	Δν(cm.⁻¹).		λ (A.).	ν (cm.⁻¹).	Δν(cm.⁻¹).	
2412	41460			2169	46100		
2387	41890		590	2165	46190		520
2378	42050	540		2145	46620	560	
2357	42430		485	2139	46750		550
2351	42535			2120	47170	560	
2323	43050		515	2114	47310		580
2294	43590		540	2100	47620		
2267	44110		520	2094	47750	550	
2240	44640		530	2089	47860		510
2217	45110		550	2072	48260		
2213	45190	530		(2063)	48470		590
2191	45640		450	(2053)	48710		
2169	46100	550	462	2047	48850		
2165	46190						

The absorption spectrum of methyldideuteramine consists of bands extending from 2410 A. to the limit of transmission of quartz. Certain of the bands at the longer wave-lengths appear to have sharp heads and to be degraded towards the violet, but in general they are diffuse. A microphotometer trace was taken from a plate obtained at a pressure of 2·5 mm. and gave indications of many weak bands in addition to those measured and recorded in Table III. There is indeed no doubt that the spectrum is complex, and the use of instruments of much higher dispersion will be necessary before a vibrational analysis can be attempted.

A general comparison of the absorption spectra of methyldideuteramine and methylamine shows that they are totally different. The bands are differently spaced and the agreement of a few values for the wave-lengths of bands is clearly fortuitous. The measurements in Table III show a constant frequency difference of about 530 cm.$^{-1}$. Deviations from this mean are such as would arise from an error of 1—2 A. in measuring the positions of the bands, except in the neighbourhood of 2200 A., where uncertainty arises probably because of confusion between bands of the two main systems and those of the subsidiary systems. There are at least two series of bands which overlap, giving some of the bands the appearance of being double.

The frequency difference of 530 cm.$^{-1}$ probably corresponds to the value of 650 cm.$^{-1}$ which was first observed by Herzberg and Kolsch in the absorption spectrum of methylamine (*Z. Elektrochem.*, 1933, **39**, 572). The origin of this characteristic vibrational frequency is not clear, but it appears to be paralleled by the differences between the observed frequencies for deuterium cyanide (570·2 cm.$^{-1}$; Bartunek and Barker, *Physical Rev.*, 1935, **48**, 516; Dadieu and Klopper, *Wiener. Anz.*, 1935, 95) and for hydrogen cyanide (712 cm.$^{-1}$; Adel and Barker, *Physical Rev.*, 1934, **45**, 277; Herzberg and Spink, *Proc. Roy. Soc.*, *A*, 1934, **147**, 434). This question has been discussed by Henri and Lasareff (*loc. cit*). Our present observations are insufficient to decide between the alternative explanations which have been suggested.

The general method here described for preparing deuteramines is being applied to isolate and examine other compounds of this type.

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29. *Studies in Dielectric Polarisation. Part XXI. The Effect of Solvent and Temperature upon the Polarisation and Apparent Moments of Bromides.*

By Eric G. Cowley and James R. Partington.

The present paper, which describes measurements on bromobenzene and ethyl bromide, is a continuation of the work reported in Part XX (Cowley and Partington, J., 1936, 1184), in which the influences of the solvent and of the temperature in a particular solvent upon the moments of two nitriles were investigated. Determinations of the polarisations and apparent moments of bromobenzene and ethyl bromide have now been made over a temperature range in six solvents, *viz.*, hexane, *cyclo*hexane, carbon tetrachloride, benzene, toluene, and carbon disulphide. Since the moments of both these bromides have been accurately determined in the vapour state, we have compared vapour values calculated from solution data by the solvent-effect equations with the experimental results for the vapours. These calculations are mentioned in a later part of the paper.

The general conclusions from the present work resemble those deduced from the experiments on the nitriles. We find that all the values of the apparent moments of bromobenzene and ethyl bromide measured in solution are smaller than the vapour values for these compounds and that, within the limit of experimental error, the polarisation values for each compound found at any one temperature in the various solvents fall as the dielectric constant of the solvent increases.

The moments of the bromides have not previously been investigated in a number of solvents under the same conditions. The earlier results are given below :

Bromobenzene : vapour 1·71 (Groves and Sugden, J., 1935, 971); in hexane 1·60 at 25° (Hampson, *Trans. Faraday Soc.*, 1934, **30**, Appendix, p. 24); in carbon tetrachloride 1·53 (temperature method) (Das and Roy, *Indian J. Physics*, 1930, **5**, 441); in benzene 1·53 at 20° (Tiganik, *Z. physikal. Chem.*, 1931, *B*, **13**, 425), 1·70 (Daily, *Physical Rev.*, 1929, **34**, 548), 1·55 at 25° (Le Fèvre and Le Fèvre, J., 1936, 1130).

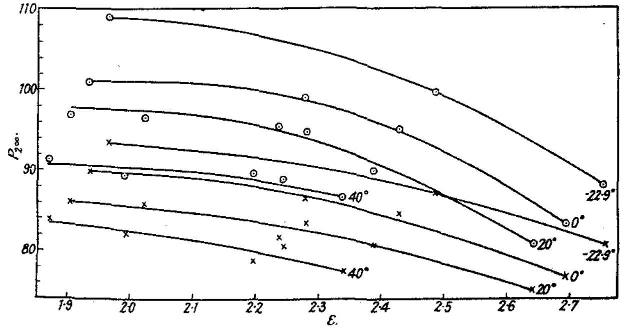
Ethyl bromide : vapour 2·02 (Smyth and McAlpine, *J. Chem. Physics*, 1934, **2**, 499), 1·99 (Mahanti, *Phil. Mag.*, 1935, **20**, 274); in hexane 1·86 (temperature method) (Smyth and Morgan, *J. Amer. Chem. Soc.*, 1928, **50**, 1547); in benzene 2·12 (Daily, *loc. cit.*). (The values of the moments are expressed here and throughout the paper in Debye units.)

The results of the present research are summarised in Table I, in which the temperature of measurement, $t°$; the solvent; the dielectric constant, ϵ, of the solvent; the polarisation of the solute at infinite dilution, $P_{2\infty}$; and the moment, μ, are given. As in the previous work, the moment has been calculated at each temperature from the difference of the total polarisation at infinite dilution and the electronic polarisation. These data may be compared with the results found in different solvents at 20° for the polarisations of chlorobenzene and *n*-propyl chloride (Müller, *Physikal. Z.*, 1933, **34**, 689) as these two compounds closely resemble the two bromides both in magnitude of moment and in molecular structure. The influence of the solvent on the polarisation is very similar for the two pairs of substances.

TABLE I.

Solute.		Bromobenzene : $P_E = 34·0$ c.c.			Ethyl bromide : $P_E = 19·1$ c.c.		
Temp. $t°$.	Solvent.	ϵ of solvt.	$P_{2\infty}$.	μ.	ϵ of solvt.	$P_{2\infty}$.	μ.
40°	C_6H_{14}	1·871	84·0	1·59	1·871	91·5	1·91
40	C_6H_{12}	1·990	82·2	1·56	1·990	89·5	1·89
40	CCl_4	2·197	78·8	1·50	2·196	89·7	1·89
40	C_6H_6	2·242	80·7	1·54	2·242	89·1	1·88
40	C_7H_8	2·339	77·5	1·48	2·338	86·8	1·84
20	C_6H_{14}	1·902	86·0	1·57	1·903	96·5	1·91
20	C_6H_{12}	2·020	86·0	1·57	2·021	96·5	1·91
20	CCl_4	2·237	81·7	1·50	2·236	95·6	1·90
20	C_6H_6	2·281	83·6	1·53	2·280	94·9	1·89
20	C_7H_8	2·386	80·8	1·49	2·385	90·0	1·83
20	CS_2	2·643	75·4	1·40	2·642	81·0	1·71
10	C_6H_{12}	2·035	87·5	1·56	2·037	98·0	1·90
10	C_6H_6	2·301	85·2	1·53	2·300	96·5	1·88
0	C_6H_{14}	1·933	90·0	1·57	1·933	101·0	1·90
0	CCl_4	2·276	86·5	1·52	2·277	99·3	1·88
0	C_7H_8	2·435	84·8	1·50	2·431	95·2	1·83
0	CS_2	2·697	77·0	1·38	2·695	85·6	1·71
−22·9	C_6H_{14}	1·966	93·5	1·55	1·965	109·0	1·90
−22·9	C_7H_8	2·488	87·2	1·47	2·485	100·0	1·81
−22·9	CS_2	2·758	81·0	1·38	2·755	89·5	1·69

The figures in Table I indicate that the moment decreases with increase of dielectric constant of the solvent at any one temperature and the polarisation values plotted against the dielectric constant show regular variations. This is the case at all the four temperatures



The variation of $P_{2\infty}$ of bromobenzene (points indicated by X) and ethyl bromide (points indicated by ⊙) with ϵ, the dielectric constant of the solvent, at various temperatures (given by the figures).

at which several measurements have been made. The results are shown in the diagram. The variations found for the bromides are much smaller, as would be expected from the magnitude of the moments, than those found in the case of the nitriles; and the variation

of the moment in a particular solvent with the temperature, found for the latter compounds, is not evident here, as the moments of the bromides determined in one solvent remain constant within the limits of experimental error over the range investigated. The difference between the moments of two aromatic and aliphatic compounds of the same type in the vapour state can be compared with the difference from solution measurements. In the present instance, this difference for the vapours of ethyl bromide and bromobenzene is 0·30, whereas the difference between the moments of these two bromides under the same conditions from the above solution measurements is 0·31—0·40.

The lines obtained by plotting the values of the total polarisation at different temperatures in each solvent against the reciprocal of the absolute temperature are straight, the deviations of the readings lying within the error of measurement. Table II gives the values of the induced polarisation, P_{E+A}, obtained by extrapolation of these lines, and the value of the apparent atomic polarisation, P_A, is found by subtracting the electronic polarisation from the intercept.

TABLE II.

Solute.	Bromobenzene.		Ethyl bromide.		Solute.	Bromobenzene.		Ethyl bromide.	
	P_{E+A},	P_A,	P_{E+A},	P_A,		P_{E+A},	P_A,	P_{E+A},	P_A,
Solvent.	c.c.	c.c.	c.c.	c.c.	Solvent.	c.c.	c.c.	c.c.	c.c.
C_6H_{14}	44	10	23	4	C_6H_6	40	6	25	6
C_6H_{12}	38	4	22	3	C_7H_8	40	6	28	9
CCl_4	37	3	27	8	CS_2	42	8	25	6

The average of these approximate values in Table II is about 6 c.c. for the apparent atomic polarisation of each of the bromides : both results are larger than the values deduced from the vapour measurements on these compounds. Smyth and McAlpine (*loc. cit.*), from measurements on ethyl bromide vapour, find P_A to be 2·9 c.c., which is considerably smaller than the earlier value found from solutions in hexane, *viz.*, 11 c.c. (Smyth and Morgan, *loc. cit.*). It has been pointed out (Smyth, *J. Chem. Physics*, 1933, **1**, 247; Smyth and McAlpine, *ibid.*, 1935, **3**, 347; Jenkins, *Trans. Faraday Soc.*, 1934, **30**, 739) that these high values of the atomic polarisation are due to the slope of the P_2–$1/T$ line, which is reduced by the change of the dielectric constant of the solvent with temperature, and thus makes the value of the intercept too large and the moment calculated from the slope too small. This is generally found to occur with the *n*-alkyl halides, so that the temperature method cannot be applied to these compounds with certainty. As explained above, we have calculated the moments at each temperature from ($P_{2\infty} - P_E$). Groves and Sugden (*loc. cit.*) take the value of the atomic polarisation of bromobenzene as 5% of P_E, *i.e.*, 1·7 c.c.

The variation of the polarisation with solvent and temperature has also been examined by Müller's method (*Physikal. Z.*, 1934, **35**, 346). When the values of $P_{O+A} \times T$, the product of the orientation polarisation and the absolute temperature of measurement, are plotted against those of ϵ, the dielectric constant of the solvent at the same temperature, a smooth curve results. The curvature is not very marked, as the variations with the dielectric constant are relatively small. The product $P_{O+A} \times T$ varies in the case of bromobenzene from $1·56 \times 10^4$ in hexane at 313° abs. to $1·18 \times 10^4$ in carbon disulphide at 250·1° abs., and for ethyl bromide from $2·27 \times 10^4$ to $1·76 \times 10^4$ under the same conditions.

It has already been mentioned that the moments of the vapours of bromobenzene and ethyl bromide are higher than the solution values. This might be expected for molecules which possess radicals on their dipole axes (Frank, *Proc. Roy. Soc.*, 1935, *A*, **152**, 171) and have positive Kerr constants (Higasi, *Bull. Inst. Phys. Chem. Res., Tokyo*, 1934, **13**, 1167).

Müller's equation (*Physikal. Z.*, 1933, **34**, 689) [see equation (1), Part XX, *loc. cit.*] is applicable to this type of molecule, and the results for the bromides at 20° have been corrected for the solvent effect by means of this equation. The calculated values of the total polarisation are given in Table III, together with that for the vapour at the same temperature. With the exception of the determinations in the anisotropic solvent carbon disulphide, the results are reasonably consistent and give average values of the total polarisation of 89·7 c.c. and 103·5 c.c. for bromobenzene and ethyl bromide, respectively. These correspond with moments of 1·60 and 1·99 respectively, whereas the experimental vapour values are 1·71 and 2·01. (The former two moments have been corrected for the atomic polarisation,

on the assumption that P_A is 5% of P_E, so that the experimental vapour moments are comparable with the calculated values.) The agreement in the latter case is good, while in the former the calculated value is the smaller, but as the moment is somewhat smaller here, the same errors in the calculation would be relatively more serious. It may be noted that the results of solution measurements on chlorobenzene on correction by Müller's equation give values lower than that for the vapour of this compound. Thus, data in nine solvents give calculated vapour values of 1·62—1·67, with a mean value of 1·65, a little lower than the vapour value of 1·70 (McAlpine and Smyth, *J. Chem. Physics*, 1935, **3**, 55).

TABLE III.

Values of $P_{2\ vapour}$ calculated from the data at 20° by (*a*) Müller's and (*b*) Sugden's equation.

Solute.	Bromobenzene.		Ethyl bromide.	
Solvent.	(*a*).	(*b*).	(*a*).	(*b*).
C_6H_{14}	89·4	101·6	101·5	119·8
C_6H_{12}	90·4	103·7	103·1	122·8
CCl_4	87·9	101·4	105·5	127·1
C_6H_6	90·7	104·8	105·5	127·2
C_7H_8	88·9	102·4	101·9	122·7
CS_2	85·9	98·1	96·7	114·9
Mean (excepting value in CS_2)	89·7	102·8	103·5	123·9
Vapour value	97·6		106·4	

Calculations have also been made by using Sugden's equation (*Trans. Faraday Soc.*, 1934, **30**, 720) [see equation (2), Part XX] and the values so obtained are included in Table III. The variations between individual values calculated from results in different solvents are not large, with the exception of the values from carbon disulphide solutions. In the results of Table III no allowance has been made for the constant α of Sugden's equation. The mean values of the total polarisation of bromobenzene and ethyl bromide from Table III are 102·8 c.c. and 123·9 c.c. respectively. To make these values correspond with the vapour results of 97·6 c.c. and 106·4 c.c. respectively, the constant α would be about 5 c.c. for bromobenzene and 17 c.c. for ethyl bromide. These constants are only approximate, as they are mean values from determinations in a number of solvents.

In Part XX (*loc. cit.*) the equation (5), deduced by Govinda Rau (*Proc. Indian Acad. Sci.*, 1935, *A*, **1**, 498) from the theory of Raman and Krishnan (*Proc. Roy. Soc.*, 1928, *A*, **117**, 589) for a solution of a polar substance in a non-polar solvent, was applied to the results, and it was shown that the polarisation value corrected for solvent influences was, in the case of benzonitrile, nearly equal to that deduced from Müller's equation. We have used the equation in the present research, making assumptions for bromobenzene similar to those previously used for benzonitrile. The constants used for ethyl bromide and the solvents are taken from published data (Govinda Rau, *loc. cit.*; Krishnan and Rao, *Indian J. Physics*, 1929—30, **4**, 39; Ramanadham, *Proc. Indian Acad. Sci.*, 1934, *A*, **1**, 281) and are given in Table V. In the calculations, the values of the moments of bromobenzene and ethyl bromide are taken as 1·6 and 1·9 respectively. The calculated values are given in Table IV. (For definitions of the symbols in Tables IV and V, see Part XX, p. 1188.)

TABLE IV.

Solvent.	$P_{2\infty}$, c.c., soltn.	$-N\Psi_1\frac{3\alpha\epsilon_1}{(\epsilon_1+2)^2}$.	$-N\Psi_2\frac{\epsilon_1-1}{\epsilon_1+2}$.	$\frac{-N\Theta}{3kT}\cdot\frac{\epsilon_1-1}{\epsilon_1+2}$.	P_2, c.c., vapour.
		Bromobenzene: at 20°.			
C_6H_{14}	86·0	0·7	1·0	3·6	91·3
C_6H_{12}	86·0	0·8	1·1	3·9	91·8
CCl_4	81·7	0	1·3	4·5	87·5
C_6H_6	83·6	1·8	1·3	4·6	91·3
CS_2	75·4	1·0	1·6	5·5	81·5
		Ethyl bromide: at 20°.			
C_6H_{14}	96·5	0·4	0·4	3·4	100·7
C_6H_{12}	96·5	1·4	0·4	3·7	102·0
CCl_4	95·6	0	0·5	4·3	100·4
C_6H_6	94·9	2·6	0·5	4·4	102·4
CS_2	81·0	1·5	0·6	5·2	88·2

The average of the calculated values of the polarisation in the first four solvents for bromobenzene is 90·5 c.c., with a corresponding moment, corrected for P_A, of 1·61, while the experimental vapour value is 1·71. The most significant correction in the above calculations is the third term involving Θ (assumed equal to $\mu^2 s_1$). If it is assumed that the whole of the difference between the calculated and the experimental vapour polarisations is due to error in this term, a value of s_1 can be calculated from the vapour value of the polarisation. From the foregoing results for bromobenzene in hexane and benzene, s_1 is found to be about $-2·5$, of the same order as but larger than the value assumed in the calculations. Govinda Rau (*loc. cit.*) has already pointed out that the value of s_1 found in this way for some other compounds is larger than the figure deduced from theoretical considerations and used in the calculations. It seems, therefore, that in several cases the calculated value of the term $\mu^2 s_1$ is somewhat smaller than is necessary to account for its contribution to the difference between the solution and vapour values, a view in agreement with that expressed by Frank (*Chem. and Ind.*, 1936, **14**, 37). In view of the approximate nature of the treatment and the uncertainty in the constants involved in the calculations, the calculated and the experimental moments are reasonably close. The corresponding calculated values for the total vapour polarisation and moment corrected for P_A are 101·4 c.c. and 1·96 for ethyl bromide, whereas the experimental vapour moment is 2·01, in better agreement than in the case of bromobenzene.

TABLE V.

Solvent.	s_1.	s_2.	s_3.	$a_1 \times 10^{23}$.	$a_2 \times 10^{23}$.	$a_3 \times 10^{23}$.
C_6H_{14}	−1·78	0·89	0·89	1·44	1·07	1·07
C_6H_{12}	−0·75	−0·75	1·5	1·31	1·31	0·98
CCl_4	0	0	0	—	—	—
C_6H_6	−1·21	−1·21	2·42	1·41	1·41	0·71
CS_2	−0·91	0·46	0·46	1·43	0·59	0·59
C_6H_5Br	—	—	—	1·85	1·85	0·93
C_2H_5Br	−0·81	0·40	0·40	1·26	0·91	0·91

The method of Higasi (*Sci. Papers Inst. Phys. Chem. Res., Japan*, 1936, **28**, 284) can be used to find the relation between experimental and theoretical values of $\Sigma\mu_i/\mu$, where $\Sigma\mu_i$ is the sum of the induced moments produced by dissolving the molecule in a solvent, and μ is the dipole moment in the vapour state. The two compounds now being considered are somewhat similar in molecular structure to the two nitriles previously investigated, and fall into the same category as the latter compounds, having values of $k > 1$ and thus a negative value of A. [See equations (6)—(9); Part XX.] As no figures for k are available, the values of k assumed are : for bromobenzene 1·65 (Higasi, *loc. cit.*), and for ethyl bromide 1·3 (that of methyl bromide : the values for ethyl chloride and methyl chloride are approximately the same; cf. Stuart, "Molekülstructur," Berlin, 1934, pp. 221, 234). The calculated and experimental values of $\Sigma\mu_i/\mu$ are collected in Table VI, together with the necessary data for the solvents (all results relating to 20°). All the solution values of the moments in Table VI have been corrected for the atomic polarisation, taken as 5% of the electronic polarisation. The calculated values in the case of carbon disulphide, which are lower than the others, being omitted, the average values of the calculated vapour moments are 1·66 and 1·99 for bromobenzene and ethyl bromide respectively, compared with the experimental vapour values of 1·71 and 2·01.

TABLE VI.

Solute.		Bromobenzene ($A = -0·112$).				Ethyl bromide ($A = -0·0673$).			
			$\Sigma\mu_i/\mu$.				$\Sigma\mu_i/\mu$.		
Solvent.	$4\pi\nu\alpha$.	μ, exptl.	Exptl.	Calc.	$\mu_{vap.}$, calc.	μ, exptl.	Exptl.	Calc.	$\mu_{vap.}$, calc.
(Vapour)	—	1·71	—	—	—	2·01	—	—	—
C_6H_{14}	0·693	1·54	−0·10	−0·08	1·68	1·90	−0·05	−0·05	2·00
C_6H_{12}	0·761	1·54	−0·10	−0·08	1·68	1·90	−0·05	−0·05	2·00
CCl_4	0·876	1·47	−0·14	−0·10	1·64	1·89	−0·06	−0·05	1·99
C_6H_6	0·898	1·50	−0·12	−0·10	1·67	1·88	−0·06	−0·06	2·00
C_7H_8	0·948	1·46	−0·14	−0·11	1·65	1·82	−0·09	−0·06	1·94
CS_2	1·062	1·37	−0·20	−0·12	1·58	1·70	−0·15	−0·07	1·84

The main uncertainty in the application of these last two theoretical formulæ is the evaluation of the difficultly accessible constants. In view of the approximations made to obtain these constants, the calculated figures for the vapour moments are on the whole in fairly satisfactory quantitative agreement with the experimental results.

EXPERIMENTAL.

The apparatus and technique employed in the present research have been described in preceding papers in this series (Cowley and Partington, J., **1935**, 604; **1936**, 1184).

Preparation of Materials.—Bromides. Bromobenzene (Kahlbaum) was purified by fractionating it twice through a column. The properties were: b. p. 155·0°/756 mm., $D_{4°}^{20°}$ 1·4950, $n_D^{20°}$ 1·5600, $[R_L]_D^{20°}$ 33·96 c.c. Figures for comparison are: b. p. 155·6°/760 mm. (Weger, *Annalen*, 1883, **221**, 71); 155·0°, corr. (Perkin, J., 1896, **69**, 1248); 154·6—155·0°/741·9 mm.; $D_{4°}^{20°}$ 1·4914, $n_D^{20°}$ 1·5598 (Brühl, *Annalen*, 1880, **200**, 187); $D_{4°}^{20°}$ 1·4953 (Biron, *Chem. Zentr.*, 1910, **14**, I, 1912); b. p. 155·4—155·6°/760 mm., $D_{4°}^{20°}$ 1·4946, $n_D^{20°}$ 1·5600 (Bugarsky, *Z. physikal. Chem.*, 1910, **71**, 712). Ethyl bromide (Kahlbaum) was twice shaken with concentrated sulphuric acid and separated. It was washed with distilled water several times, dried over calcium chloride, and twice fractionated. Its physical properties were: b. p. 38·2°/755 mm., $D_{4°}^{20°}$ 1·4600, $n_D^{20°}$ 1·4244, $[R_L]_D^{20°}$ 19·06 c.c. Previous determinations are: b. p. 38·4°/760 mm. (Timmermans, *Chem. Zentr.*, 1911, **15**, II, 1015; Tyrer, J., 1914, **105**, 2538), $D_{4°}^{20°}$ 1·45983 (Patterson and Thomson, J., 1908, **93**, 371), 1·4555, $n_D^{20°}$ 1·42386 (Weegmann, *Z. physikal. Chem.*, 1888, **2**, 231), $D_{4°}^{20°}$ 1·4586 (Smyth and Morgan, *J. Amer. Chem. Soc.*, 1928, **50**, 1547), $n_D^{20°}$ 1·4239 (I. C. T.).

Solvents. With the exception of hexane ("from petroleum"), which was obtained from Kahlbaum, the solvents were obtained from the same sources and were purified as described in Part XX (*loc cit.*).

Results.—The symbols and method of calculation are those previously employed in this series. The moments are calculated at each temperature from $P_{2\infty}$ minus P_E, P_A being included with the orientation polarisation. The solvent and temperature of each measurement are stated.

Solute: Bromobenzene.

In hexane at 40°.

f_2.	ϵ.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	1·871	0·6566	29·52	—
0·014459	1·905	0·6666	30·31	83·7
0·027657	1·936	0·6755	31·02	83·6
0·039897	1·965	0·6839	31·66	83·0
0·053721	1·997	0·6935	32·35	82·2

$P_{2\infty}$ = 84·0 c.c.; P_E = 34·0 c.c.; $P_{2\infty} - P_E$ = 50·0 c.c.; μ = 1·59.

In hexane at 20°.

f_2.	ϵ.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	1·902	0·6746	29·52	—
0·014459	1·938	0·6845	30·33	85·7
0·027657	1·972	0·6939	31·07	85·6
0·039897	2·003	0·7022	31·75	85·3
0·053721	2·039	0·7119	32·50	85·0

$P_{2\infty}$ = 86·0 c.c.; P_E = 34·0 c.c.; $P_{2\infty} - P_E$ = 52·0 c.c.; μ = 1·57.

In hexane at 0°.

f_2.	ϵ.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	1·933	0·6925	29·51	—
0·014459	1·973	0·7026	30·38	89·6
0·027657	2·010	0·7119	31·17	89·6
0·039897	2·044	0·7204	31·88	89·0
0·053721	2·082	0·7303	32·65	87·9

$P_{2\infty}$ = 90·0 c.c.; P_E = 34·0 c.c.; $P_{2\infty} - P_E$ = 56·0 c.c.; μ = 1·57.

In hexane at −22·9°.

f_2.	ϵ.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	1·966	0·7115	29·49	—
0·014459	2·010	0·7221	30·40	92·9
0·027657	2·052	0·7322	31·24	92·8
0·039897	2·090	0·7415	31·98	91·8
0·053721	2·133	0·7512	32·82	91·6

$P_{2\infty}$ = 93·5 c.c.; P_E = 34·0 c.c.; $P_{2\infty} - P_E$ = 59·5 c.c.; μ = 1·55.

In *cyclo*hexane at 40°.

f_2.	ϵ.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	1·990	0·7596	27·48	—
0·010995	2·019	0·7670	28·07	81·5
0·021436	2·047	0·7741	28·64	81·4
0·032298	2·076	0·7813	29·22	81·3
0·041673	2·100	0·7878	29·68	80·4

$P_{2\infty}$ = 82·2 c.c.; P_E = 34·0 c.c.; $P_{2\infty} - P_E$ = 48·2 c.c.; μ = 1·56.

In *cyclo*hexane at 20°.

f_2.	ϵ.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·020	0·7781	27·43	—
0·010995	2·052	0·7853	28·08	86·0
0·021436	2·082	0·7924	28·66	84·8
0·032298	2·114	0·8000	29·27	84·4
0·041673	2·141	0·8065	29·78	85·0

$P_{2\infty}$ = 86·0 c.c.; P_E = 34·0 c.c.; $P_{2\infty} - P_E$ = 52·0 c.c.; μ = 1·57.

In *cyclo*hexane at 10°.

f_2.	ϵ.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·035	0·7874	27·41	—
0·010995	2·069	0·7950	28·07	87·4
0·021436	2·101	0·8023	28·67	86·3
0·032298	2·133	0·8099	29·27	85·2
0·041673	2·162	0·8165	29·81	85·0

$P_{2\infty}$ = 87·5 c.c.; P_E = 34·0 c.c.; $P_{2\infty} - P_E$ = 53·5 c.c.; μ = 1·56.

In carbon tetrachloride at 40°.

f_2.	ϵ.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·197	1·5557	28·21	—
0·009065	2·223	1·5550	28·66	78·2
0·020477	2·257	1·5544	29·23	78·4
0·030396	2·288	1·5537	29·75	79·1
0·039254	2·314	1·5530	30·20	78·9

$P_{2\infty}$ = 78·8 c.c.; P_E = 34·0 c.c.; $P_{2\infty} - P_E$ = 44·8 c.c.; μ = 1·50.

In carbon tetrachloride at 20°.

f_2.	ε.	$D^{t°}_{4°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·237	1·5940	28·18	—
0·009065	2·266	1·5932	28·66	81·6
0·020477	2·303	1·5919	29·27	81·7
0·030396	2·335	1·5908	29·80	81·5
0·039254	2·365	1·5902	30·28	81·7

$P_{2\infty}$ = 81·7 c.c.; P_E = 34·0 c.c.; $P_{2\infty} - P_E$ = 47·7 c.c.; μ = 1·50.

In benzene at 40°.

f_2.	ε.	$D^{t°}_{4°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·242	0·8577	26·65	—
0·010889	2·278	0·8656	27·24	80·7
0·020779	2·310	0·8729	27·76	79·9
0·031199	2·344	0·8802	28·31	79·7
0·040406	2·375	0·8866	28·81	80·0

$P_{2\infty}$ = 80·7 c.c.; P_E = 34·0 c.c.; $P_{2\infty} - P_E$ = 46·7 c.c.; μ = 1·54.

In benzene at 10°.

f_2.	ε.	$D^{t°}_{4°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·301	0·8893	26·56	—
0·010889	2·342	0·8973	27·19	84·6
0·020779	2·380	0·9046	27·77	84·7
0·031199	2·419	0·9122	28·35	84·1
0·040406	2·454	0·9190	28·87	83·8

$P_{2\infty}$ = 85·2 c.c.; P_E = 34·0 c.c.; $P_{2\infty} - P_E$ = 51·2 c.c.; μ = 1·53.

In toluene at 20°.

f_2.	ε.	$D^{t°}_{4°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·386	0·8662	33·60	—
0·011377	2·418	0·8730	34·13	80·5
0·022612	2·451	0·8801	34·66	80·3
0·033160	2·481	0·8864	35·14	80·1
0·043308	2·511	0·8929	35·60	79·9

$P_{2\infty}$ = 80·8 c.c.; P_E = 34·0 c.c.; $P_{2\infty} - P_E$ = 46·8 c.c.; μ = 1·49.

In toluene at −22·9°.

f_2.	ε.	$D^{t°}_{4°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·488	0·9058	33·71	—
0·011377	2·527	0·9127	34·31	86·5
0·022612	2·567	0·9197	34·91	86·6
0·033160	2·605	0·9262	35·47	86·7
0·043308	2·640	0·9327	35·96	85·7

$P_{2\infty}$ = 87·2 c.c.; P_E = 34·0 c.c.; $P_{2\infty} - P_E$ = 53·2 c.c.; μ = 1·47.

In carbon disulphide at 0°.

f_2.	ε.	$D^{t°}_{4°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·697	1·2929	21·27	—
0·011036	2·751	1·2969	21·89	77·0
0·021846	2·802	1·3009	22·47	76·2
0·030500	2·849	1·3044	22·98	76·0
0·042312	2·906	1·3090	23·61	76·5

$P_{2\infty}$ = 77·0 c.c.; P_E = 34·0 c.c.; $P_{2\infty} - P_E$ = 43·0 c.c.; μ = 1·38.

In carbon tetrachloride at 0°.

f_2.	ε.	$D^{t°}_{4°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·276	1·6326	28·11	—
0·009065	2·309	1·6320	28·64	86·4
0·020477	2·351	1·6309	29·30	86·0
0·030396	2·387	1·6296	29·86	85·8
0·039254	2·420	1·6290	30·36	85·4

$P_{2\infty}$ = 86·5 c.c.; P_E = 34·0 c.c.; $P_{2\infty} - P_E$ = 52·5 c.c.; μ = 1·52.

In benzene at 20°.

f_2.	ε.	$D^{t°}_{4°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·281	0·8787	26·59	—
0·010889	2·320	0·8866	27·20	83·2
0·020779	2·356	0·8938	27·76	83·2
0·031199	2·395	0·9010	28·37	83·1
0·040406	2·427	0·9078	28·86	82·7

$P_{2\infty}$ = 83·6 c.c.; P_E = 34·0 c.c.; $P_{2\infty} - P_E$ = 49·6 c.c.; μ = 1·53.

In toluene at 40°.

f_2.	ε.	$D^{t°}_{4°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·339	0·8478	33·52	—
0·011377	2·368	0·8548	34·01	76·9
0·022612	2·397	0·8616	34·50	76·9
0·033160	2·426	0·8680	34·98	77·6
0·043308	2·453	0·8746	35·41	77·1

$P_{2\infty}$ = 77·5 c.c.; P_E = 34·0 c.c.; $P_{2\infty} - P_E$ = 43·5 c.c.; μ = 1·48.

In toluene at 0°.

f_2.	ε.	$D^{t°}_{4°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·435	0·8846	33·69	—
0·011377	2·472	0·8918	34·27	84·5
0·022612	2·507	0·8988	34·82	83·7
0·033160	2·539	0·9056	35·37	84·3
0·043308	2·573	0·9115	35·82	82·8

$P_{2\infty}$ = 84·8 c.c.; P_E = 34·0 c.c.; $P_{2\infty} - P_E$ = 50·8 c.c.; μ = 1·50.

In carbon disulphide at 20°.

f_2.	ε.	$D^{t°}_{4°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·643	1·2633	21·32	—
0·011036	2·691	1·2672	21·91	74·8
0·021846	2·741	1·2716	22·50	75·0
0·030500	2·778	1·2746	22·95	74·5
0·042312	2·831	1·2791	23·57	74·5

$P_{2\infty}$ = 75·4 c.c.; P_E = 34·0 c.c.; $P_{2\infty} - P_E$ = 41·4 c.c.; μ = 1·40.

In carbon disulphide at −22·9°.

f_2.	ε.	$D^{t°}_{4°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·758	1·3247	21·23	—
0·011036	2·819	1·3286	21·88	80·0
0·021846	2·881	1·3326	22·53	80·5
0·030500	2·928	1·3359	23·01	79·7
0·042312	2·992	1·3405	23·68	79·1

$P_{2\infty}$ = 81·0 c.c.; P_E = 34·0 c.c.; $P_{2\infty} - P_E$ = 47·0 c.c.; μ = 1·38.

Solute: Ethyl bromide.

In hexane at 40°.

f_2.	ε.	$D^{t°}_{4°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	1·871	0·6568	29·51	—
0·010815	1·901	0·6612	30·18	91·2
0·021909	1·932	0·6658	30·85	90·5
0·031863	1·960	0·6700	31·43	89·9
0·040300	1·985	0·6736	31·94	89·8

$P_{2\infty}$ = 91·5 c.c.; P_E = 19·1 c.c.; $P_{2\infty} - P_E$ = 72·4 c.c.; μ = 1·91.

In hexane at 0°.

f_2.	ε.	$D^{t°}_{4°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	1·933	0·6925	29·51	—
0·010815	1·971	0·6976	30·28	101·0
0·021909	2·010	0·7029	31·05	99·8
0·031863	2·045	0·7073	31·73	99·3
0·040300	2·078	0·7115	32·34	99·8

$P_{2\infty}$ = 101·0 c.c.; P_E = 19·1 c.c.; $P_{2\infty} - P_E$ = 81·9 c.c.; μ = 1·90.

In hexane at 20°.

f_2.	ε.	$D^{t°}_{4°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	1·903	0·6748	29·54	—
0·010815	1·937	0·6796	30·26	96·1
0·021909	1·972	0·6844	30·98	95·4
0·031863	2·005	0·6890	31·64	95·6
0·040300	2·033	0·6930	32·17	95·0

$P_{2\infty}$ = 96·5 c.c.; P_E = 19·1 c.c.; $P_{2\infty} - P_E$ = 77·4 c.c.; μ = 1·91.

In hexane at −22·9°.

f_2.	ε.	$D^{t°}_{4°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	1·965	0·7133	29·39	—
0·010815	2·006	0·7175	30·24	107·6
0·021909	2·050	0·7232	31·06	105·7
0·031863	2·089	0·7279	31·79	104·6
0·040300	2·124	0·7324	32·40	104·0

$P_{2\infty}$ = 109·0 c.c.; P_E = 19·1 c.c.; $P_{2\infty} - P_E$ = 89·9 c.c.; μ = 1·90.

In *cyclo*hexane at 40°.

f_2.	ε.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	1·990	0·7596	27·48	—
0·011198	2·028	0·7649	28·16	88·4
0·022499	2·066	0·7694	28·85	88·6
0·033081	2·102	0·7740	29·49	88·1
0·044380	2·142	0·7793	30·15	87·8

$P_{2\infty}$ = 89·5 c.c.; P_E = 19·1 c.c.; $P_{2\infty} - P_E$ = 70·4 c.c.; μ = 1·89.

In *cyclo*hexane at 10°.

f_2.	ε.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·037	0·7876	27·44	—
0·011198	2·082	0·7926	28·23	97·7
0·022499	2·127	0·7976	28·99	96·5
0·033081	2·170	0·8026	29·70	95·8
0·044380	2·217	0·8076	30·46	95·4

$P_{2\infty}$ = 98·0 c.c.; P_E = 19·1 c.c.; $P_{2\infty} - P_E$ = 78·9 c.c.; μ = 1·90.

In carbon tetrachloride at 20°.

f_2.	ε.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·236	1·5941	28·16	—
0·011285	2·288	1·5932	28·91	94·5
0·020309	2·330	1·5923	29·50	94·1
0·032703	2·387	1·5911	30·27	92·7
0·043769	2·438	1·5901	30·95	91·9

$P_{2\infty}$ = 95·6 c.c.; P_E = 19·1 c.c.; $P_{2\infty} - P_E$ = 76·5 c.c.; μ = 1·90.

In benzene at 40°.

f_2.	ε.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·242	0·8577	26·65	—
0·010361	2·288	0·8625	27·30	89·1
0·020265	2·332	0·8673	27·90	88·3
0·029903	2·375	0·8720	28·47	87·5
0·039828	2·421	0·8767	29·10	88·0

$P_{2\infty}$ = 89·1 c.c.; P_E = 19·1 c.c.; $P_{2\infty} - P_E$ = 70·0 c.c.; μ = 1·88.

In benzene at 10°.

f_2.	ε.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·300	0·8891	26·55	—
0·010361	2·354	0·8940	27·27	96·2
0·020265	2·407	0·8990	27·95	95·7
0·029903	2·458	0·9039	28·58	94·7
0·039828	2·513	0·9089	29·25	94·4

$P_{2\infty}$ = 96·5 c.c.; P_E = 19·1 c.c.; $P_{2\infty} - P_E$ = 77·4 c.c.; μ = 1·88.

In toluene at 20°.

f_2.	ε.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·385	0·8664	33·57	—
0·011197	2·430	0·8710	34·20	89·7
0·022016	2·474	0·8757	34·78	88·7
0·032097	2·516	0·8801	35·33	88·4
0·042638	2·560	0·8845	35·89	88·1

$P_{2\infty}$ = 90·0 c.c.; P_E = 19·1 c.c.; $P_{2\infty} - P_E$ = 70·9 c.c.; μ = 1·83.

In toluene at −22·9°.

f_2.	ε.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·485	0·9058	33·65	—
0·011197	2·544	0·9119	34·38	98·6
0·022016	2·596	0·9163	35·04	96·4
0·032097	2·645	0·9203	35·64	95·6
0·042638	2·695	0·9250	36·22	93·4

$P_{2\infty}$ = 100·0 c.c.; P_E = 19·1 c.c.; $P_{2\infty} - P_E$ = 80·9 c.c.; μ = 1·81.

In carbon disulphide at 0°.

f_2.	ε.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·695	1·2925	21·26	—
0·011142	2·779	1·2955	21·98	85·6
0·021769	2·858	1·2978	22·65	84·8
0·032732	2·941	1·3005	23·32	84·1
0·042396	3·015	1·3027	23·91	83·7

$P_{2\infty}$ = 85·6 c.c.; P_E = 19·1 c.c.; $P_{2\infty} - P_E$ = 66·5 c.c.; μ = 1·71.

In *cyclo*hexane at 20°.

f_2.	ε.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·021	0·7783	27·45	—
0·011198	2·064	0·7833	28·21	95·8
0·022499	2·107	0·7884	28·95	94·6
0·033081	2·148	0·7936	29·63	93·4
0·044380	2·193	0·7985	30·37	93·3

$P_{2\infty}$ = 96·5 c.c.; P_E = 19·1 c.c.; $P_{2\infty} - P_E$ = 77·4 c.c.; μ = 1·91.

In carbon tetrachloride at 40°.

f_2.	ε.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·196	1·5556	28·19	—
0·011285	2·242	1·5549	28·88	88·7
0·020309	2·279	1·5542	29·41	88·1
0·032703	2·330	1·5529	30·13	87·6
0·043769	2·376	1·5522	30·77	87·0

$P_{2\infty}$ = 89·7 c.c.; P_E = 19·1 c.c.; $P_{2\infty} - P_E$ = 70·6 c.c.; μ = 1·89.

In carbon tetrachloride at 0°.

f_2.	ε.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·277	1·6327	28·13	—
0·011285	2·335	1·6319	28·94	99·4
0·020309	2·380	1·6310	29·54	97·5
0·032703	2·444	1·6298	30·37	96·7
0·043769	2·503	1·6293	31·11	96·2

$P_{2\infty}$ = 99·3 c.c.; P_E = 19·1 c.c.; $P_{2\infty} - P_E$ = 80·2 c.c.; μ = 1·88.

In benzene at 20°.

f_2.	ε.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·280	0·8787	26·57	—
0·010361	2·332	0·8838	27·28	94·3
0·020265	2·381	0·8884	27·93	93·3
0·029903	2·430	0·8933	28·55	92·6
0·039828	2·482	0·8983	29·19	92·3

$P_{2\infty}$ = 94·9 c.c.; P_E = 19·1 c.c.; $P_{2\infty} - P_E$ = 75·8 c.c.; μ = 1·89.

In toluene at 40°.

f_2.	ε.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·338	0·8480	33·49	—
0·011197	2·379	0·8527	34·07	85·8
0·022016	2·418	0·8570	34·62	85·1
0·032097	2·455	0·8612	35·12	84·4
0·042638	2·493	0·8657	35·62	83·4

$P_{2\infty}$ = 86·8 c.c.; P_E = 19·1 c.c.; $P_{2\infty} - P_E$ = 67·7 c.c.; μ = 1·84.

In toluene at 0°.

f_2.	ε.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·431	0·8848	33·61	—
0·011197	2·482	0·8897	34·29	94·6
0·022016	2·532	0·8944	34·94	94·1
0·032097	2·577	0·8988	35·50	92·6
0·042638	2·627	0·9034	36·12	92·5

$P_{2\infty}$ = 95·2 c.c.; P_E = 19·1 c.c.; $P_{2\infty} - P_E$ = 76·1 c.c.; μ = 1·83.

In carbon disulphide at 20°.

f_2.	ε.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·642	1·2632	21·33	—
0·011142	2·716	1·2657	21·99	80·6
0·021769	2·787	1·2681	22·62	80·6
0·032732	2·861	1·2705	23·26	80·4
0·042396	2·927	1·2728	23·82	80·0

$P_{2\infty}$ = 81·0 c.c.; P_E = 19·1 c.c.; $P_{2\infty} - P_E$ = 61·9 c.c.; μ = 1·71.

In carbon disulphide at −22·9°.

f_2.	ε.	$D_{4°}^{t°}$.	P_{12}, c.c.	P_2, c.c.
0·000000	2·755	1·3260	21·19	—
0·011142	2·849	1·3301	21·93	87·7
0·021769	2·938	1·3335	22·62	86·7
0·032732	3·032	1·3365	23·33	86·5
0·042396	3·113	1·3394	23·92	85·6

$P_{2\infty}$ = 89·5 c.c.; P_E = 19·1 c.c.; $P_{2\infty} - P_E$ = 70·4 c.c.; μ = 1·69.

SUMMARY.

The apparent moments and polarisations of bromobenzene and ethyl bromide in six solvents have been measured over a temperature range. It has been found that all the values of the moments in solution are lower than the vapour results and that the polarisation at each temperature decreases with increase of the dielectric constant of the solvent. The figures have been examined by the solvent-effect equations and it is concluded that the agreement between the calculated values and the experimental vapour determinations is on the whole fairly satisfactory.

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30. *Studies in Solvent Action. Part XII. Optical Rotatory Powers of* l-*Benzoin and* l-*Benzoin Methyl Ether in Solution.*

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THE data already published in this series of communications show that the rotatory power of an optically active compound is profoundly modified by the association of the active compound with itself or with a solvent. This process is facilitated by the presence in the solvent and solute molecules of polar substituent groups. For a weakly polar solute dissolved in a large excess of solvent the association is mainly of solute–solvent type and varies with the polarity of the solvent, being of a high order of magnitude in strongly polar media and either very low or entirely absent in those of non-polar type. If the optically active molecules are strongly polar, they will in addition have a pronounced tendency to associate with themselves, both in the homogeneous state and when dissolved in a non-polar medium. In interpreting the optical changes it has been assumed that the electrical field exerted by a polar group upon the active molecule to which it is attached makes its own characteristic contribution towards the total rotatory power. Dipole association between this group and a neighbouring polar group—whether belonging to a similar molecule or to one of an added substance—would thus be expected to result in a diminution of the electrical contribution and in a corresponding alteration in optical rotation. In practice it has been observed that both the above types of association lead to optical displacements in the same direction, in accordance with the requirements of this hypothesis.

These investigations have now been extended by an examination of *l*-benzoin and its methyl ether. The former is chiefly of interest owing to its property of readily undergoing association in certain non-polar solvents: the methyl ether has a smaller power of self-association, but may yield dextro- or lævo-rotatory solutions according to the experimental conditions.

l-*Benzoin*.—A reliable comparison of the relative degrees of association of benzoin in different non-polar solvents is not easily achieved by use of the classical methods, as the solubility of the compound is low and the necessary measurements cannot be made at the same temperature. Determinations by the ebullioscopic method (see p. 144) have, however, been carried out in *cyclo*hexane, carbon tetrachloride, benzene, and carbon disulphide. In *cyclo*hexane the molecules of benzoin (*M.W.* 212) are found to be strongly associated even at low concentrations, the calculated molar weight rising rapidly from 238 at $c = 0{\cdot}371$ to 274 at $c = 1{\cdot}037$. In carbon tetrachloride and benzene the values rose steadily though less rapidly over similar ranges of concentration, but in carbon disulphide they remained constant within the experimental limits. The rotatory powers of *l*-benzoin dissolved in various solvents are given in Table I. For reasons already stated (J., 1931, 674—679) it is considered preferable to tabulate aromatic and aliphatic solvents separately.

In the present case the main factors controlling the magnitude of the optical rotation appear to be the refractive index of the medium and the degree of association of the active

molecules with themselves or with molecules of the solvent. The refractive effect is revealed in the tendency of the rotatory powers to rise as the refractive index increases, a change which is in agreement with modern theories of optical activity although the relationship is often so dominated by polar and other factors as to be scarcely traceable. The polar influence is marked by the low rotations observed in strongly polar liquids and the high values found in those of less polar character.

TABLE I

Molecular Rotations of l-*Benzoin in Solution.*

Solvent.	$[M]_{5461}^{20°}$.	μ.	$n_D^{20°}$.	Solvent.	$[M]_{5461}^{20°}$.	μ.	$n_D^{20°}$.
Acetaldehyde	−276°	2·7	1·332	Acetophenone	−460°	2·9	1·533
Acetone	314	2·8	1·359	Nitrobenzene	462	3·9	1·550
Acetonitrile	413	3·2	1·344	Benzaldehyde	513	2·7	1·545
Nitromethane	427	3·0	1·381	Benzonitrile	530	3·8	1·528
Methanol	427	1·7	1·328	Mesitylene	550	0	1·496
*cyclo*Hexane	464	0	1·427	Toluene	568	0·4	1·495
Methylene chloride	534	1·5	1·424	Benzene	571	0	1·501
Chloroform	545	1·0	1·446	Bromobenzene	619	1·5	1·560
Acetic acid	585	1·7	1·372	Chlorobenzene	627	1·5	1·525
Methyl iodide	625	1·3	1·530	Anisole	649	1·2	1·516
Carbon tetrachloride	633	0	1·461	Iodobenzene	700	1·2	1·618
Carbon disulphide	1064	0	1·628				

In the majority of cases $l = 2$ and $c = 2$ (approx.). For some solvents a lower concentration was necessary, *viz.*, methanol ($c = 1·012$), acetic acid ($c = 1·010$), *cyclo*hexane ($c = 0·056$; $l = 4$), carbon disulphide ($c = 0·522$), carbon tetrachloride ($c = 0·22$), nitrobenzene ($c = 1·037$), mesitylene ($c = 0·966$), toluene ($c = 0·81$), benzene ($c = 1·01$), bromobenzene ($c = 0·986$). Observed rotations varied from −0·49° (*cyclo*hexane) to −13·60° (iodobenzene). Values of the dipole moments, μ, and refractive indices of the pure solvents are also appended.

Aromatic solvents illustrate the polar influence very clearly, as the variations in their refractive indices are on a smaller scale than those occurring among the aliphatic derivatives. The depression in rotatory power produced by highly polar liquids is also evident from a general survey of the aliphatic and aromatic solvents employed. Thus, although the refractive indices, $n_D^{20°}$, of the four highly polar benzene derivatives from acetophenone to benzonitrile all lie between the relatively high limits 1·528 and 1·550, the corresponding rotatory powers of their solutions follow immediately after those of the most strongly polar aliphatic solvents and assume a position between methanol ($n_D^{20°}$ 1·328) and methylene chloride ($n_D^{20°}$ 1·424). Here the polar influence outweighs that due to the refractive power.

Among non-polar liquids, *cyclo*hexane yields solutions of the lowest rotatory power, as was to be anticipated from the fact that benzoin is most strongly associated in this solvent. A displacement in the same direction is also observed with the hydrocarbons mesitylene, toluene, and benzene. In carbon disulphide no appreciable association of the solute could be detected at low concentrations by the ebullioscopic method, and the solution has a very high rotatory power in agreement with its high refractive index and non-polar character.

Weakly polar solvents, it may be noted, also yield solutions of relatively high optical activity. In such media the intermolecular forces are assumed to be sufficiently powerful to prevent the aggregation of *l*-benzoin molecules at low concentrations, but not strong enough to depress the rotatory power greatly by the formation of solute–solvent complexes. To take a concrete example, the degree of solvation which occurs in the weakly polar methyl iodide is regarded as producing an optical depression of the same order as that due to the self-association of the benzoin molecules in carbon tetrachloride solution. Neither of these solutions shows a rotatory power as high as that which would be given by *l*-benzoin if it could exist in the truly unimolecular state at the same temperature in a non-polar medium. In some respects the case of *l*-benzoin resembles that of *d*-β-nitro-octane (Rule, Smith, and Harrower, J., 1933, 376), which is very strongly associated and exhibits its highest rotations in solvents of intermediate polarity. With the latter compound, however, no refractivity effect could be traced, probably owing to the extremely high polarity of the nitro-group and its greater tendency to undergo association in solvents of all kinds.

TABLE II.

l-*Benzoin Methyl Ether in Solution* (l = 2, c = 4).

Solvent.	$[M]^{20°}_{5461}$.	μ.	$n^{20°}_{D}$.	Solvent.	$[M]^{20°}_{5461}$.	μ.	$n^{20°}_{D}$.
Methanol	−352°	1·7	1·328	Aniline	−374°	1·6	1·586
Acetic acid	−344	1·7	1·372	Benzonitrile	−146	3·8	1·528
Nitromethane	−320	3·0	1·381	Benzaldehyde	−125	2·7	1·545
Acetaldehyde	−243	2·7	1·332	Nitrobenzene	−117	3·9	1·550
Acetonitrile	−236	3·2	1·344	Acetophenone	−109	2·9	1·533
Chloroform	−214	1·0	1·446	*o*-Dichlorobenzene	− 8·0	2·2	1·549
Methylene chloride	−178	1·5	1·424	Anisole	+ 6·6	1·2	1·516
Acetone	−102	2·8	1·359	Bromobenzene	+ 35	1·5	1·560
Methyl iodide	+ 27	1·3	1·530	Chlorobenzene	+ 35	1·5	1·525
Carbon tetrachloride	+316	0	1·461	Iodobenzene	+ 43	1·2	1·618
Carbon disulphide	+370	0	1·628	Benzene	+138	0	1·501
*cyclo*Hexane	+373	0	1·427	Toluene	+190	0·4	1·495
				Mesitylene	+269	0	1·496

α_{5461} varied from 0·23° in anisole to 13·29° in *cyclo*hexane. Owing to the low rotatory powers in *o*-dichlorobenzene, a concentration of $c = 10$ was used; the rotation in this solvent was found to be negative for λ_{6563}, λ_{5893}, and λ_{5761}, but positive for λ_{4861} and λ_{4358}.

l-*Benzoin Methyl Ether.*—Preliminary determinations of the molecular weight of *l*-benzoin methyl ether in *cyclo*hexane and benzene by the ebullioscopic method indicated very little self-association. The compound is readily soluble in all types of solvents to form solutions varying from a high lævo- to a high dextro-rotation, and it will be observed (Table II) that, with the sole exception of aniline, all solvents giving higher negative rotations than − 150° possess low refractive indices. The relationship between refractive index and rotatory power is, however, irregular, as may be seen from the positions in the table occupied by the highly refractive compounds aniline (− 374°), iodobenzene (+ 43°), and carbon disulphide (+ 370°), and also from the very high dextrorotations recorded in the remaining non-polar liquids, all of which have refractive indices of intermediate values. In fact, among the aromatic solvents as a group, no definite refractive influence is visible, although there is a clear connexion between rotatory power and the polarity of the medium.

Whereas all the strongly polar solvents give lævorotatory solutions, aniline at the head of the list occupies a higher position than corresponds to its dipole moment. This is probably to be attributed to an abnormal electronic coupling between its amino-group and the ketonic group of the benzoin ether. The rotatory powers in aniline were found to fall very slowly, owing either to combination between solvent and solute or to racemisation in the weakly basic medium. The general resemblance between hydroxy- and amino-groups may account for the similarly high rotations found for the hydroxylic solvents methanol and acetic acid. With both aliphatic and aromatic solvents, however, the compounds of non-polar character are sharply differentiated from adjacent solvents in the tables by the very highly dextrorotatory nature of their solutions. *l*-Benzoin methyl ether has also been examined in the homogeneous state at temperatures ranging from 55° to 100°. When extrapolated to 20°, the determinations give a value for $[M]_{5461}$ of approximately − 99°. Thus the rotatory power of the ketonic ether in the absence of any solvent is practically identical with that found for a solution in either of the ketonic solvents acetone (− 102°) or acetophenone (− 109°). In view of the widely differing refractive indices of these two liquids, this coincidence further emphasises the importance of the chemical character of the solvent in its influence upon the rotatory power.

Influence of Concentration.—The molecular rotatory powers for *l*-benzoin in Table I indicate a fall in the negative rotation as the degree of association is raised by dissolution of the compound in strongly polar solvents. A similar change is therefore to be anticipated when solutions of *l*-benzoin are examined at increasing concentrations in a non-polar solvent. This is found to be the case; *e.g.*, in benzene solutions, $[M]^{20°}_{5461}$ falls from −571° at $p = 1·146$ to − 559° at $p = 2·831$.

Concentration effects over a wider range are, however, readily investigated with the more soluble *l*-benzoin methyl ether. From Table II it is seen that a rise in the degree of association of this compound, as brought about by solution in solvents of greater dipole

moment, corresponds to an increase in the negative rotatory power. In agreement with this relationship, a rise in the concentration of a solution in benzene displaces the dextrorotation towards the negative region :

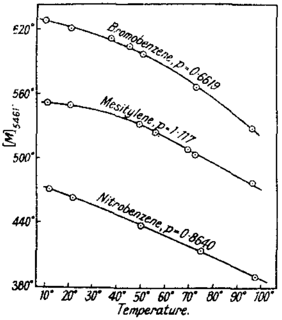
l-*Benzoin Methyl Ether in Benzene.*

c	0·643	4·02	12·02	25·05	Homog. state *
$[\alpha]_{5893}^{20°}$	+50·9°	+ 47·0°	+ 39·1°	+26·7°	−35·4°
$[M]_{5461}^{20°}$	—	+138°	+115°	+80·1°	−99°

* Extrapolated from the data obtained for the fused ether (see later). The value at c = 0·643 is that recorded by Wren for 15° (J., 1909, **95**, 1584).

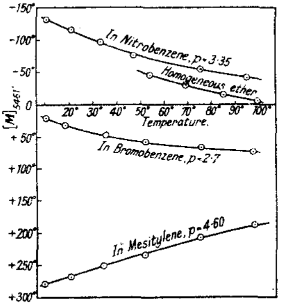
Influence of Temperature.—It has been pointed out (Rule, J., 1933, 1222) that the theory of dipoles allows a prediction to be made as to the relative slopes of the temperature-rotation curves for highly polar and for non-polar solvents, in those cases where a definite relationship is traceable between the polarity of a solvent and the rotatory power of the solution. Since the degree of dipole association between solvent and solute generally

FIG. 1.



Rotatory power of l-*benzoin in solution.*

FIG. 2.



Rotatory power of l-*benzoin methyl ether.*

diminishes as the temperature rises, it follows that the characteristic optical displacement due to a highly polar solvent will also diminish. The T–R curves for polar and non-polar solvents will therefore tend to converge with rise of temperature.

Owing to the association of the optically active molecules with one another, *l*-benzoin exhibits somewhat abnormal rotatory powers when dissolved in the majority of non-polar solvents. The above prediction should, however, hold equally well if a weakly polar solvent capable of disrupting the solute–solute complexes is substituted for one of non-polar type. This is illustrated in Fig. 1, which shows the influence of a rise in temperature upon the rotatory powers of *l*-benzoin in the three solvents bromobenzene, mesitylene, and nitrobenzene. It will be observed that the curve for the strongly polar nitrobenzene converges towards that for the weakly polar bromobenzene, the difference in the values of $[M]_{5461}$ falling from 156° at 20° to 131° at 100°. The curve for the non-polar solvent mesitylene occupies an intermediate position.

l-Benzoin methyl ether (Fig. 2) shows the effect even more clearly, since in this case the degree of association of the solute molecules in non-polar solvents is small and the comparison can be made under more favourable conditions. Here the curves for nitrobenzene, bromobenzene, and mesitylene are arranged in the order of their dipole moments and converge rapidly with rise of temperature, apparently trending towards positions on the

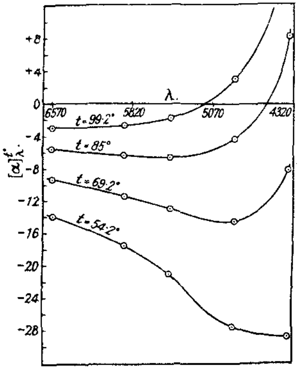
positive side of the diagram. The curve for the homogeneous optically active compounc which as a ketonic ether may be assumed to have a dipole moment not far removed fror 2·9, falls into its proper place below that of nitrobenzene and is inclined in the same genera direction.

In cases where a definite influence due to the refractive index of the medium is visibl at low temperatures, this should become still more clearly defined as the temperature i raised and the degree of association falls. No such tendency can be traced in the above ver limited data.

Nature of the Dispersion.—The diagram obtained by plotting the rotatory powers o *l*-benzoin against the wave-length of light in the visible region shows the dispersion in al solvents to be normal and complex. For bromobenzene and chlorobenzene the dispersioı curves lie close together and cut one another in the neighbourhood of λ_{4845}; a similar inter section about λ_{5520} occurs with acetophenone and nitrobenzene.

l-Benzoin methyl ether in solution exhibits a more interesting type of dispersion, th curves lying partly in the negative and partly in the positive region (see data in experimenta section). In *o*-dichlorobenzene ($c = 10$) th rotatory powers are negative for wave-length longer than 4935 A., and positive for shorte wave-lengths up to λ_{4358}. For the methyl ethe in the homogeneous state between 55° and 100 the dispersion is either highly complex o anomalous according to the conditions, as i illustrated in Fig 3. This complexity in th optical properties, however, does not appreci ably disturb the relationship existing betweeı the rotatory power and the polarity of th solvent.

FIG. 3.



Optical rotatory dispersion of homogeneous l-benzoin methyl ether.

EXPERIMENTAL.

l-Benzoin was prepared from amygdalin by wa of *d*-mandelonitrile (Smith, *Ber.*, 1931, **64**, 427) Yields were similar to those recorded by thi worker, the purified product having m. p. 131—132 and $[\alpha]_D^{16°} = -119·2°$ in acetone ($c = 2·76$) (Smitl quotes $-119·4°$ for $c = 2·50$). Methylation o *l*-benzoin was effected according to Wren (*loc. cit.*) by means of dry silver oxide and methyl iodide ir acetone. The resulting methyl *l*-benzoin had th same rotatory power as that found by Wren.

Solvents were purified in the manner describec in earlier papers of this series. Refractive indices are taken from "Critical Constants" and refer to the D-line, the corresponding values foı λ_{5461} not being generally available. No correction has been made for the changes in refractive index produced by the addition of optically active solute, which will in any case be small in magnitude.

Observed Optical Rotations.

l-Benzoin ($l = 2$, $t = 20°$, all rotations negative).

Solvent.	*c*.	α_{6563}.	α_{5893}.	α_{5461}.	α_{4861}.	α_{4358}.
Acetaldehyde	2·328	−3·78°	−4·96°	−6·07°	−8·68°	−12·86°
Acetone	2·764	5·07	6·59	8·18	11·84	17·90
Acetonitrile	2·262	5·53	7·14	8·82	12·64	18·85
Nitromethane	2·306	5·76	7·47	9·29	13·33	20·05
Methyl alcohol	1·012	2·55	3·30	4·08	5·86	8·68
Methylene chloride............	2·288	7·41	9·56	11·77	16·72	24·62
Chloroform	2·212	7·18	9·39	11·55	16·43	24·03
Acetic acid	1·010	3·57	4·56	5·57	7·86	11·41
Methyl iodide	2·216	8·30	10·66	13·08	18·53	27·01
Carbon tetrachloride	0·220	0·84	1·09	1·32	1·86	2·73
Carbon disulphide	0·522	3·32	4·28	5·24	7·44	10·75

Solvent.	c.	α_{6563}.	α_{5893}.	α_{5461}.	α_{4861}.	α_{4358}.
Acetophenone	2·036	5·53°	7·15°	8·83°	12·57°	18·57°
Nitrobenzene *	1·037	1·38	1·80	2·26	3·27	—
*cyclo*Hexane	0·047	—	—	0·42	—	0·950
	0·056	—	—	0·49	—	1·13
Benzaldehyde	2·314	6·87	9·01	11·19	16·10	24·03
Benzonitrile	2·324	7·28	9·40	11·61	16·52	24·35
Mesitylene	0·966	1·54	1·99	2·51	3·54	5·19
Toluene	0·810	2·72	3·54	4·34	6·16	9·03
Benzene	1·012	3·37	4·43	5·44	7·69	11·24
Bromobenzene	0·986	1·80	2·33	2·88	4·14	6·1
Chlorobenzene	2·068	7·70	9·95	12·24	17·35	25·37
Anisole	2·082	7·98	10·36	12·75	17·97	26·23
Iodobenzene	2·058	8·59	11·05	13·60	19·19	28·23

* $t = 21·5°$.

l-Benzoin methyl ether ($l = 2$, $t = 20°$).

Solvent.	c.	α_{6563}.	α_{5893}.	α_{5461}.	α_{4861}.	α_{4358}.
Methyl alcohol	4·022	−7·68°	−10·10°	−12·53°	−17·97°	−27·05°
Acetic acid	4·020	−7·53	− 9·91	−12·25	−17·29	−25·36
Nitromethane	4·014	−5·39	− 7·20	− 9·04	−13·36	−20·75
Acetaldehyde	4·020	−5·35	− 7·05	− 8·66	−12·28	−17·95
Acetonitrile	4·006	−4·97	− 6·65	− 8·38	−12·32	−19·22
Chloroform	4·020	−4·84	− 6·24	− 7·63	−10·75	−15·45
Methylene chloride	4·018	−3·91	− 5·14	− 6·32	− 8·88	−12·84
Acetone	4·030	−2·18	− 2·89	− 3·65	− 5·46	− 8·51
Methyl iodide	4·036	+0·35	+ 0·62	+ 0·98	+ 2·06	+ 5·14
Carbon tetrachloride	4·026	+6·46	+ 8·82	+11·25	+17·46	+30·23
Carbon disulphide	4·012	+7·58	+10·25	+13·15	+20·34	+35·07
Benzonitrile	4·064	−3·21	− 4·23	− 5·26	− 7·64	−11·57
Benzaldehyde	4·010	−2·79	− 3·65	− 4·45	− 6·36	− 9·08
Nitrobenzene †	4·018	−1·25	− 1·67	− 2·07	− 2·96	—
Acetophenone	4·016	−2·17	− 3·16	− 3·88	− 5·98	− 7·97
o-Dichlorobenzene	10·04	−0·90	− 0·91	− 0·80	+ 0·03	+ 3·88
Anisole	4·008	+0·05	+ 0·11	+ 0·23	+ 0·79	+ 2·53
Bromobenzene *	3·984	+0·25	+ 0·37	+ 0·58	+ 1·17	+ 2·80
Chlorobenzene	4·020	+0·58	+ 0·89	+ 1·26	+ 2·35	+ 5·35
Iodobenzene	4·026	+0·71	+ 1·06	+ 1·53	+ 2·94	+ 6·76
Benzene	4·022	+2·81	+ 3·78	+ 4·91	+ 7·84	+14·34
Toluene	4·022	+3·82	+ 5·24	+ 6·76	+10·52	+18·49
Mesitylene †	4·021	+2·77	+ 3·75	+ 4·84	+ 7·39	+12·57
*cyclo*Hexane	4·022	+7·68	+10·32	+13·29	+20·18	+34·31

* $l = 1$, $t = 18·2°$. † $l = 1$.

Influence of Temperature.

l-Benzoin in nitrobenzene ($l = 1$, $p = 0·8640$).

Temp.	12°	21·5°	50°	74·5°	97·7°
$d_{4°}^{t°}$	1·209	1·200	1·173	1·150	1·129
α_{5461}	−2·32°	−2·26°	−2·09°	−1·94°	−1·79°

l-Benzoin in bromobenzene ($l = 1$, $p = 0·6619$).

Temp.	10·5°	21°	38°	45·5°	51°	73°	96·5°
$d_{4°}^{t°}$	1·504	1·491	1·469	1·460	1·452	1·424	1·393
α_{5461}	−2·95°	−2·88°	−2·80°	−2·76°	−2·70°	−2·51°	−2·30°

l-Benzoin in mesitylene ($l = 1$, $p = 1·117$).

Temp.	11°	20·5°	49·5°	55·5°	69·5°	72·5°	96·5°
$d_{4°}^{t°}$	0·8737	0·8655	0·8427	0·8379	0·8267	0·8245	0·8052
α_{5461}	−2·54°	−2·51°	−2·36°	−2·31°	−2·21°	−2·18°	−2·02°

l-Benzoin methyl ether in nitrobenzene ($l = 1$, $p = 3·354$).

Temp.	10·5°	21°	35·5°	47·2°	75·5°	94·5°
$d_{4°}^{t°}$	1·209	1·198	1·187	1·174	1·147	1·128
α_{6563}	−1·44°	−1·25°	—	−0·79°	—	−0·47°
α_{5893}	−1·91	−1·67	—	−1·09	—	−0·59
α_{5461}	−2·40	−2·07	−1·72°	−1·32	−0·92°	−0·68
α_{4861}	−3·55	−2·96	—	−1·78	—	−0·79

l-Benzoin methyl ether in bromobenzene ($l = 1$, $p = 2{\cdot}699$).

Temp.	10·2°	18·2°	35·5°	52·2°	73·5°	97·2°
$d_{4°}^{t°}$	1·488	1·476	1·456	1·435	1·409	1·379
α_{6563}	+0·13°	+0·25°	+0·42°	+0·50°	+0·58°	+0·62°
α_{5893}	+0·25	+0·37	+0·59	+0·73	+0·83	+0·91
α_{5461}	+0·39	+0·58	+0·83	+1·00	+1·13	+1·22
α_{4861}	+0·89	+1·17	+1·57	+1·75	+1·96	+2·06
α_{4358}	+2·18	+2·80	+3·31	+3·67	+4·01	+4·18

l-Benzoin methyl ether in mesitylene ($l = 1$, $p = 4{\cdot}604$).

Temp.	9·5°	20·5°	34·5°	52°	75°	97·2°
$d_{4°}^{t°}$	0·8825	0·8735	0·8625	0·8480	0·8295	0·8110
α_{6563}	+2·92°	+ 2·76°	+ 2·59°	+ 2·35°	+2·08°	+1·84°
α_{5893}	+3·93	+ 3·71	+ 3·46	+ 3·15	+2·76	+2·44
α_{5461}	+5·00	+ 4·79	+ 4·43	+ 4·08	+3·51	+3·13
α_{4861}	+7·67	+ 7·30	+ 6·84	+ 6·27	+5·51	+4·83
α_{4358}	—	+12·44	+11·61	+10·73	+9·62	+8·63

l-Benzoin methyl ether, homogeneous state ($l = 0{\cdot}5$).

Temp.	$d_{4°}^{t°}$.	α_{6563}.	α_{5893}.	α_{5461}.	α_{4861}.	α_{4358}.
54·2°	1·094	−7·64°	−9·64°	−11·48°	−15·18°	−15·71°
69·2	1·083	−5·07	−6·18	− 7·07	− 7·91	− 4·39
85·6	1·070	−3·00	−3·43	− 3·54	− 2·37	+ 4·47
99·2	1·059	−1·58	−1·43	− 0·94	+ 1·63	+11·37(?)

Determinations of Molecular Weight.—These were carried out by using the differential thermometer devised by Menzies and Wright (*J. Amer. Chem. Soc.*, 1921, **43**, 2314). In the following tables: c = concn./100 c.c. of solvent; Δt = elevation in b. p.

l-*Benzoin* (M.W. 212).

Wt. of solute, g.	c.	Δt.	M.	Wt. of solute, g.	c.	Δt.	M.
		In benzene. Vol. 27·9 c.c.; b. p. 80·0°; $K = 32$.					
0·1356	0·4860	0·0754°	206	0·4688	1·680	0·2506°	214
0·2739	0·9817	0·1501	209	0·6570	2·355	0·3375	223
		In carbon tetrachloride. Vol. 29·1 c.c.; b. p. 76·3°; $K = 32{\cdot}4$.					
0·0786	0·2701	0·0444	196	0·2863	0·9840	0·1563	204
0·1761	0·6050	0·0990	198	0·3790	1·302	0·2018	209
		In cyclohexane. Vol. 28·4 c.c.; b. p. 81·3°; $K = 27{\cdot}5$.					
0·1053	0·3708	0·0593	238	0·2946	1·037	0·1471	274
0·1992	0·7015	0·1091	246				
		In carbon disulphide. Vol. 27·5 c.c.; b. p. 45·6°; $K = 19{\cdot}4$.					
0·1784	0·6503	0·0574	219	0·3204	1·165	0·1033	215
0·2437	0·8861	0·0785	219				

l-Benzoin Methyl Ether (M.W. 226).

Wt. of solute, g.	c.	Δt.	M.	Wt. of solute, g.	c.	Δt.	M.
		In benzene. Vol. 29 c.c.; b. p. 79·6°; $K = 32$.					
0·2361	0·8141	0·1156	225	0·4371	1·508	0·2164	223
0·3334	1·149	0·1673	220	0·5462	1·884	0·2668	226
		In cyclohexane. Vol. 28 c.c.; b. p. 80°; $K = 27{\cdot}5$.					
0·2656	0·9705	0·1492	243	0·5547	1·981	0·2967	255
0·4179	1·492	0·2273	251				

Summary.

An examination of the optical rotatory powers exhibited by *l*-benzoin and its methyl ether when dissolved in a variety of solvents leads to the following conclusions.

1. The lævorotation of *l*-benzoin tends to rise in solvents of high refractive index and to fall in those of high dipole moment. Low rotations are also observed in certain non-polar solvents in which the solute molecules undergo appreciable self-association.

2. The lævorotation of *l*-benzoin methyl ether rises in strongly polar solvents: high dextrorotations are given in all non-polar media. In this case the refractive effect is irregular.

3. The optical changes in polar solvents are due to dipole-association between solvent and solute, and displacements in the same direction occur when the concentration of the solute in a non-polar medium is increased.

4. With rising temperatures the rotatory powers observed in highly polar solvents approximate more closely to those found in solvents of zero or low dipole moment, in agreement with the demands of the association hypothesis.

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UNIVERSITY OF EDINBURGH. [*Received, December 4th, 1936.*]

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31. *Studies in Solvent Action. Part XIII. Optical Rotatory Power and the Refractive Index of the Medium.*

By H. GORDON RULE and ANGUS R. CHAMBERS.

ALL the optically active solutes previously discussed in these communications have been polar in type, and under suitable conditions their molecules readily enter into association with one another or with those of an added solvent. Although numerous active compounds of low polarity are available in the unsaturated hydrocarbons of the terpene group, very few examples of non-polar saturated hydrocarbons have yet been isolated in the optically pure state. The latter class is of particular interest from the standpoint of solvent influence, since it is to be expected that the rotatory powers of their solutions will be largely independent of the polar nature of the solvent medium. This conclusion has now been tested in the case of *d*-pinane, which may be prepared by the catalytic hydrogenation of *d*-pinene under high pressure. At the same time the properties of the unsaturated hydrocarbons *d*-pinene and *d*-limonene have also been investigated.

d-*Pinane*.*—The molecular rotatory powers found for *d*-pinane are tabulated in order of ascending magnitudes in Table I; they include observations for the hydrocarbon in the homogeneous state and in solution in 35 solvents of widely different types ranging from derivatives of methane, benzene, and naphthalene to pyridine and quinoline. As the work progressed, it became evident that the changes in optical rotation were in fact mainly dependent upon the refractive index of the medium, and in order to make a more quantitative test of this relationship the determinations were repeated with 26 selected solvents, the refractive indices of the solutions being also measured, since it is this property and not the refractive power of the pure solvent which is of theoretical significance. For the dilute solutions employed, however, the resulting corrections in the values of $n_D^{20°}$ were only of the order of $\pm$ 0·002 in average cases, with a maximum of $\pm$ 0·008 for liquids of very high or very low refractive indices. The maximum probable errors in the determinations of the molecular rotatory power are estimated to be $\pm$ 0·4° in solutions of lower and $\pm$ 0·3° in those of higher optical activity.

Influence of the Refractive Index.—The data recorded in the table show a well-marked tendency for the rotatory powers to rise as the refractive index of the solution increases, although the agreement is interrupted by many minor displacements, most of which are too large to be attributable to experimental error. One of the non-polar solvents employed, carbon tetrachloride, has a refractive index of practically the same value as *d*-pinane itself, and correspondingly it is found that dilution with this medium has no appreciable influence upon the molecular rotation of the active compound. On the other hand, the absence of any pronounced polar effect is shown in the impartial distribution throughout the table of solvents of zero and of extremely high dipole moments.

In the theoretical treatment of optical activity, the refractive index of the solvent medium has long been regarded as one of the fundamental factors governing the magnitude

* A preliminary note on the results obtained with *d*-pinane has been published in *Nature*, 1934, **133**, 910.

TABLE I.

Rotatory Powers of d-*Pinane in Solution.*

Solvent.	$n_D^{20°}$.	μ.	$[M]_D^{20°}$.	Solvent.	$n_D^{20°}$.	μ.	$[M]_D^{20°}$.
*Acetonitrile	1·3441	3·21	25·8	Benzene	1·4992	0	32·9
Methyl alcohol	1·3266	1·68	26·4	*Acetophenone*	1·5310	2·97	33·2
*Acetic acid	1·3718	1·73	26·9	Benzaldehyde	1·5431	2·75	33·2
Nitromethane	1·3864	3·05	27·3	*Toluene*	1·4930	0·4	33·7
Pentane	1·3640	0	27·4	Anisole	1·5141	1·25	34·5
*Acetaldehyde	1·3316	2·72	27·7	Chlorobenzene	1·5229	1·56	34·7
Hexane	1·3835	0	27·8	*o*-Dichlorobenzene	1·5466	2·24	34·7
Acetone	1·3653	2·76	28·9	*α-Chloronaphthalene	1·6332	1·59	34·9
*Methylene chloride	1·4245	1·51	29·0	Bromobenzene	1·5580	1·56	35·1
Chloroform	1·4489	1·05	30·2	*α-Bromonaphthalene	1·6558	1·58	35·1
Benzonitrile	1·5255	3·85	30·8	Ethylene dibromide	1·6303	1·0	35·3
Methylene bromide	1·5385	1·89	31·4	Iodobenzene	1·6162	1·25	35·6
(Homogeneous)	1·4630	0	31·5	*α-Naphthyl methyl ether	1·6201	1·3	35·6
Carbon tetrachloride	1·4616	0	31·6	Aniline	1·5842	1·60	36·4
*Pyridine	1·5088	2·11	32·3	Methylene iodide	1·7341	1·10	36·6
Mesitylene	1·4944	0	32·5	*Quinoline	1·6246	2·11	38·6
Nitrobenzene	1·5468	3·90	32·5	Carbon disulphide	1·6246	0	38·7
Methyl iodide	1·5291	1·35	32·6	*α-Iodonaphthalene	1·7054	1·43	39·7

* For these solvents the values of $n_D^{20°}$ are those given for the pure compounds in "Critical Constants"; otherwise the values are those observed for the corresponding solutions of *d*-pinane. In general, $l = 2$ and $c = 3·3$ (approx.), but lower concentrations were necessary with nitromethane ($c = 1·97$; $\alpha_D = 0·78°$) and acetonitrile ($c = 2·55$; $\alpha_D = 0·97°$). For methylene iodide, $l = 1$, $\alpha_D = 0·73°$. *The remaining values of* α_D lay *between* 1·49° *and* 2·63°.

of the rotatory power, but the relationship has never been established satisfactorily on an experimental basis. As is clear from the evidence adduced in earlier papers of this series, one reason for this failure lies in the remarkably large optical variations arising from changes in the state of association of the active compound in solution.

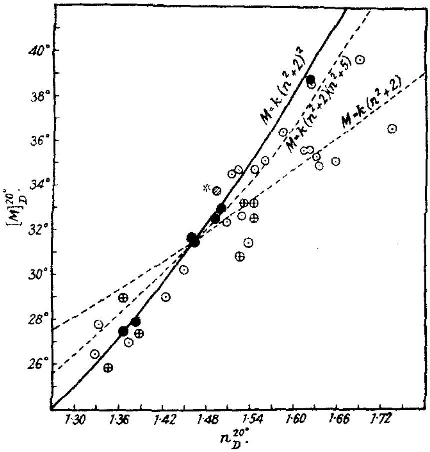
Mathematical expressions for the rotatory power which involve the refractive index of the medium have been derived on theoretical grounds by several workers. Thus Born in 1915 proposed a formula which for the limited purposes of this discussion may be simplified to $M = k_1(n^2 + 2)^2$. This was later modified by Gans, and more recently by Born himself (*Proc. Roy. Soc.*, 1935, **150**, *A*, 84) to $M = k_2(n^2 + 2)$. The theory of de Mallemann (*Rev. gén. Sci.*, 1927, **38**, 453) expresses a relationship with $(n^2 + 2)^2$, and that of Boys (*Proc. Roy. Soc.*, 1934, **144**, *A*, 681) may be reduced to $M = k_3(n^2 + 2)(n^2 + 5)$. An examination of the rotatory power of the weakly polar *d*-limonene in solution in six solvents has been made by Wolf and Volkmann (*Z. physikal. Chem.*, 1929, *B*, **3**, 139), who claim that the results confirm the modified formula of Born in which M is related to $(n^2 + 2)$; a more extended investigation of the compound, however, affords no support to this conclusion (see p. **151**).

In the case of *d*-pinane it is evident from the sequence of refractive indices in Table I that the connexion between M and n is not entirely regular. Nevertheless, it is of interest to discover how far the experimental data are in agreement with any of the above expressions. By making use of the values of $[M]_D^{20°}$ and $n_D^{20°}$ for *d*-pinane in the homogeneous state, both of which are readily determined with accuracy, the above constants k_1, k_2, and k_3 have been calculated to be 1·837, 7·605, and 1·065 respectively. From these constants the rotatory power of any given solution may be evaluated solely from a knowledge of its refractive index. In this manner the maximum variation in $[M]_D$ for *d*-pinane in the solvents under investigation should theoretically be 20·0° from k_1, 9·4° from k_2, and 15·6° from k_3. The experimentally observed range lies between these limits, *viz.*, 13·9°.

The results are best illustrated in the form of a diagram (Fig. 1) in which rotatory powers are plotted against refractive indices; curves are also reproduced for the theoretical rotations corresponding to the three expressions under discussion. It will be seen that the curve for $M = k_2(n^2 + 2)$ passes evenly among points representing solutions of a higher refractive index than that of pinane, but lies above all those of a lower refractive power. Apart from any other consideration, this peculiarity throws some doubt upon the validity of the

$(n^2 + 2)$ relationship.* More conclusive evidence is found in the properties of the ***non-polar solutions***. On general grounds it is to be expected that a solution of a saturated hydrocarbon in a non-polar solvent will conform more closely to the theoretical than one containing a solute or solvent which is polar in type. Reference to the diagram shows that every point representing a solution in a non-polar medium lies on or very close to a smooth curve which also passes through the point for the non-polar *d*-pinane in the homogeneous state. *This curve is identical with that for the expression $M = k_1(n^2 + 2)^2$*, which therefore portrays most accurately the behaviour of such solutions. The relationship of Boys is indicated in the diagram by a curve making a small angle with the above.

FIG. 1.



The rotatory power of homogeneous d*-pinane is indicated by the meeting point of the three curves; other points refer to solutions listed in Table I. Non-polar media are shown in black (toluene, $\mu = 0·4$, is marked by an asterisk) and strongly polar media of $\mu > 3$ by crosses.*

From this point of view and the arrangement of the refractive indices in the second column of the table it appears that abnormally low rotatory powers are given with naphthalene derivatives, dibromo- and di-iodo-compounds, and all strongly polar liquids having $\mu > 3$. The pinane employed had been carefully purified, and the divergences observed in strongly polar liquids cannot be explained on the assumption that it contained a trace of *d*-pinene, because the rotatory power of the latter compound is raised and not diminished on dilution with strongly polar solvents (see p. 150). A saturated hydrocarbon, however, contains a number of extremely weak dipoles,† which while mutually cancelling one another in their behaviour towards a uniform electric field, may nevertheless react normally towards the localised charge of a dipole in a neighbouring molecule and so give rise to a minor influence of the type under discussion. Further evidence in support of this suggestion is provided by the manner in which the rotatory powers are affected by an increase in tempera-

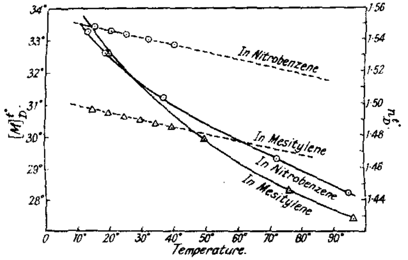
* These conclusions have been communicated to Prof. Born, who informs the authors that, according to J. M. J. Kooy (" Theorie der optische activiteit," Inaug. Diss., Leiden), a factor has been omitted from his calculations as published in 1935, the introduction of which leads to the corrected form $M = k(n^2 + 2)^2$.

† The CH– dipole has been estimated to be of the order $\mu = 0·2$.

ture. It is possible that an additional cause of irregularity in the refractivity effect in Table I lies in other variations in the state of the optically active compounds in solution, such as those due to changes in the as yet little understood van der Waals forces, or to modifications in the spatial disposition of the active molecule.

Temperature and Concentration Changes.—A temperature generalisation for an optically active compound, whose solutions vary in rotatory power with the polarity of the solvent, has already been deduced theoretically and established by experiment. In a polar medium the degree of solute-solvent association diminishes as the temperature rises, and the corresponding temperature–rotation curve therefore tends to approach the normal curve for a solution in a non-polar liquid of the same refractive index (see foregoing paper). Although the rotatory power of *d*-pinane is not closely related to the polar properties of the solvent, a weak polar influence appears to be indicated by the low rotations found in liquids of $\mu > 3$. This is borne out by the form of the *T–R* diagrams (Fig. 2) for pinane when dis-

FIG. 2.



Solutions of d-*pinane: continuous lines show rotatory powers; broken lines, refractive indices.*

solved in mesitylene and nitrobenzene severally. At low temperatures nitrobenzene, despite its greater refractive index, yields a solution of slightly smaller rotatory power than the less refractive mesitylene; but as the temperature rises the curve for nitrobenzene crosses that for mesitylene and assumes a higher position in agreement with its refractive power. Determinations of the refractive indices of these two solutions over the temperature range 15—40° show that the values are represented by two almost parallel straight lines (Fig. 2) and afford no explanation of the form of the *T–R* curves. It may thus be concluded that the reversal in the positions of the two curves at low temperatures is due to a weak polar disturbance arising from association between the hydrocarbon and the strongly polar nitrobenzene, an effect which disappears at higher temperatures. Similar disturbances may be expected to be present in other cases where the solvent is polar in character.

The typical changes in rotatory power which accompany a rise in the degree of solute–solute association are clearly shown when a polar compound such as *l*-benzoin or its methyl ether is examined at increasing concentrations in solution in a non-polar solvent. No effect of this kind is observed with *d*-pinane when dissolved in carbon disulphide, since the molecules of saturated hydrocarbons have little tendency to associate with one another. In this case the rotation–concentration diagram is found to be represented by a straight line, the slope of which corresponds to the variation in the refractive power of the solution. The linear relationship is in agreement with the fact that for two *non-polar* liquids the refractive index of the mixture is an additive property :

d-*Pinane in carbon disulphide* (t = 20°).

c	3·492 *	38·6	50·57	(Homog. pinane)
n_D	1·6246	1·5490	1·5241	1·4630
α_{5893}	1·96	9·99	12·62	19·54
$[M]_D$	38·7	35·7	34·5	31·5

* $l = 2$; in all other cases $l = 1$.

When various mixtures of carbon disulphide and the polar liquid methyl alcohol are employed as the solvent medium, with pinane added in a fixed concentration, the refractive index of the mixture is found to be less than that calculated from the proportions of the components present. Here also the variations in optical activity closely follow the changes in refractive power. The differences between the observed values and those calculated according to the three expressions discussed above are included in the table, from which it appears that a relationship involving the fourth power of the refractive index accords best with the experimental data for these solvents.

d-*Pinane* (c = ca. 3·35) *in mixtures of carbon disulphide and methanol.*

Solvent.	$n_D^{20°}$.	$[M]_D^{20°}$, obs.	($M_{obs.} - M_{calc.}$) using $(n^2 + 2)$.	$(n^2 + 2)^2$.	$(n^2 + 2)(n^2 + 5)$.
CS_2	1·6246	38·7°	+3·4	−0·85	+0·9
CS_2, 12·7 g. + CH_3·OH, 12·1 g. ...	1·4377	29·5	−1·4	−0·85	+0·75
CS_2, 6·36 g. + CH_3·OH, 8·0 g. ...	1·4162	28·8	−1·7	−0·7	+0·75
CH_3·OH	1·3266	26·4	−2·2	+0·4	−0·7

d-*Pinene*.—Unsaturated hydrocarbons, as a rule, possess exceedingly small dipole moments, but in consequence of this measurable polarity it is to be expected that in favourable cases their rotatory powers in solution will show some relation to the polar properties of the solvent. Table II contains the molecular rotations observed for *d*-pinene in the homogeneous state and for solutions in 24 solvents, the arrangement again being in ascending values of [*M*]. Clear evidence is provided in these figures of a polar as well as a refractive effect, neither of which predominates so greatly as to be free from irregularity. Thus all the lower rotations between 55° and 70° refer to solvents of zero or small dipole moment. Homogeneous *d*-pinene also falls into its proper place in this group. On the other hand, all rotations above 70° are found for solvents of medium or high polarity, chloroform being the sole exception. Superimposed upon this influence there is possibly a less definite tendency for compounds of high refractive index to form solutions of low rotatory power and *vice versa*, as appears to be shown in the order of the non-polar solvents among themselves, and in the high rotations given in the majority of media possessing small refractive indices. On this interpretation of the data carbon disulphide is an extreme example in which very high refractive index goes hand in hand with zero dipole moment, the two properties uniting to give an abnormally low activity. In acetonitrile and nitromethane the conditions are reversed, low refractive power and high polarity leading to highly active solutions. Other as yet unknown factors must also be in operation, as in the case of *d*-pinane.

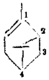
TABLE II.

d-*Pinene in Solution.*

Solvent.	$[M]_D^{20°}$.	μ.	$n_D^{20°}$.	Solvent.	$[M]_D^{20°}$.	μ.	$n_D^{20°}$.
Carbon disulphide	55·6°	0	1·6276	*o*-Dichlorobenzene	70·7°	2·24	1·5490
Methyl iodide	60·5	1·08	1·5297	Methanol	71·1	1·66	1·3284
Mesitylene	62·3	0	1·4962	Acetophenone	71·8	2·97	1·5332
Benzene	63·4	0	1·5014	Acetone......................	72·1	2·76	1·3592
*cyclo*Hexane	63·7	0	1·4273	Benzonitrile	73·4	3·85	1·5278
(Homogeneous)............	64·3	(Small)	1·4651	Acetaldehyde	73·6	2·7	1·3316
Anisole	65·2	1·25	1·5164	Methylene chloride	75·3	1·55	1·4245
Iodobenzene	65·6	1·25	1·6180	Chloroform	75·9	1·18	1·4459
Toluene	65·7	0·4	1·4950	Nitromethane	76·0	3·03	1·3815
Chlorobenzene	67·9	1·52	1·5250	Acetonitrile	76·2	3·16	1·3441
Hexane	68·9	0	1·3754	Nitrobenzene	76·2	3·90	1·5504
Carbon tetrachloride ...	69·4	0	1·4607	Acetic acid	76·4	1·73	1·3718
Aniline	70·7	1·52	1·5863				

Concentration of pinene varied from 4·016 to 4·212, and observed values of α from 3·39° to 4·70° (l = 2) (homogeneous pinene, $\alpha_D^{20°}$ = 20·48°, l = 0·5). The refractive indices quoted are those of the pure solvents.

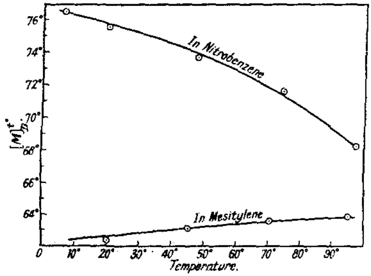
Pinene therefore differs from the great majority of the optically active compounds already examined in exhibiting a rotatory power which is *raised* in solvents of strong polarity. A tentative explanation of this peculiarity may be sought in the nature of the two centres of asymmetry in the pinene molecule and in their relative distances from the double bond. If, for example, the rotatory power is made up of a strong dextro-contribution from atom 4 and a weak lævo-contribution from atom 2, then the influence of a strongly polar solvent as transmitted through the double bond would act chiefly on the nearer asymmetric atom 2, probably depressing its characteristic lævo-contribution and resulting in an increased molecular dextrorotation.



The analysis of the experimental data being assumed to be correct, the refractive influence is also unusual, as the highest rotatory powers are given in solvents of low refractive index. Such a relationship is contrary to the requirements of current theories of optical activity, but the results of the present investigation show that these can only be expected to apply to non-polar optically active compounds in a non-polar medium. Another exception of this kind has already been found in the case of *d*-bromo-octane in aliphatic solvents (J., 1933, 377).

Concentration and Temperature Changes.—In view of the low polarity of unsaturated hydrocarbons, it is not unexpected to find that the variations in the rotatory power of *d*-

FIG. 3.



Temperature–rotation diagram for d-*pinene.*

pinene with change of concentration in a *non-polar* solvent depend chiefly upon the refractive index of the mixture. This can be deduced directly from Table II. When *d*-pinene ($n_D^{20°}$ = 1·4651) is diluted with a solvent of higher refractive power, such as carbon disulphide, mesitylene, or benzene, the optical rotation is diminished; and when the diluting medium has a lower refractive power, as with hexane or carbon tetrachloride, the rotation is raised. For the last solvent the value of n is not appreciably less than that of pinene itself, and the magnitude of the optical change on dilution may be due in part to other causes, such as the presence in the molecule of four polar CCl groups. Probably the small inversion in the relative positions of the *cyclo*hexane solution and homogeneous pinene in the table is to be attributed to a minor disturbance in the refractive influence arising from the weakly polar character of pinene, leading to a somewhat higher rotation for the homogeneous compound than for a solution in a saturated hydrocarbon of approximately the same refractive index. When rotatory powers are plotted against concentrations in these non-polar solvents, smooth curves are obtained in place of the straight-line relationship found with pinane. This difference emphasises the polar character of pinene.

The existence of optical effects due to the polarity as well as the refractive index of the medium may also be traced in the temperature–rotation curves over the range 20—90° for solutions of *d*-pinene in mesitylene and nitrobenzene (Fig. 3). In the former solvent the rotatory power increases slightly with rise of temperature, whereas in the latter it decreases

rapidly. It is obvious that the two curves will cross at a still higher temperature and so reverse the order of the rotatory powers. The conclusions deduced from the data in Table II being borne in mind, it appears that at lower temperatures the chief factor governing the position and form of the nitrobenzene curve in Fig. 3 is the strong polarity of the solvent. This results in association between solute and solvent, which in the case of *d*-pinene leads to a higher optical rotation. With rise of temperature the degree of association diminishes and the refractive power of the solvent then tends to assume a leading rôle. Since the optical rotation of pinene is lowered in solvents of high refractive index, the *T–R* curve for nitrobenzene falls towards the mesitylene curve, eventually crossing it to take up a lower position.

d-*Limonene*.—The rotatory powers of limonene in solution are given in Table III, from which it is seen that the optical rotation is controlled mainly by the refractive index of the medium in such a manner that high refractive power corresponds to high molecular rotation. This relationship is not without a considerable degree of irregularity, even when the comparison is limited to solutions in non-polar media. Not only does carbon tetrachloride yield a solution of much lower activity than was to have been expected from the value of *n*, but hexane and *cyclo*hexane, although differing appreciably in refractive power, yield solutions of practically identical molecular rotations. *d*-Limonene in the homogeneous condition possesses a refractive index of intermediate magnitude, but its rotatory power in this state is greater than that found for any of its solutions in non-polar solvents, not even excepting the very highly refractive carbon disulphide. For these reasons *d*-limonene cannot be regarded as a suitable compound for testing the relationship existing between *M* and *n*, and little weight can therefore be attached to the work of Wolf and Volkmann (*loc. cit.*) in this connexion.

The dispersions of the hydrocarbons in question have been described in the literature and are not further discussed in this communication.

TABLE III.

Rotatory Powers of d-*Limonene in Solution.*

Solvent.	$[M]_D^{20°}$.	μ.	$n_D^{20°}$.	Solvent.	$[M]_D^{20°}$.	μ.	$n_D^{20°}$.
Methanol	149·5°	1·66	1·3284	Benzene	165·5°	0	1·5014
Acetonitrile	150·8	3·16	1·3441	Carbon disulphide	166·6	0	1·6276
Carbon tetrachloride	154·4	0	1·4607	Methyl iodide	166·8	1·08	1·5297
Acetone	154·5	2·76	1·3592	Anisole	167·3	1·23	1·5164
Acetaldehyde	156·6	2·68	1·3316	Benzonitrile	167·3	3·94	1·5278
Chloroform	156·8	1·18	1·4459	(Homogeneous)	168·9	(0·5)	1·4713
Hexane	157·3	0	1·3754	Chlorobenzene	169·2	1·52	1·5250
*cyclo*Hexane	157·9	0	1·4273	Acetophenone	169·5	2·97	1·5332
Methylene chloride	158·0	1·55	1·4245	*o*-Dichlorobenzene	170·5	2·24	1·5490
Nitromethane	158·3	3·03	1·3815	Benzaldehyde	170·8	2·75	1·5453
Acetic acid	158·7	1·73	1·3718	Aniline	172·5	1·52	1·5863
Toluene	165·2	0·37	1·4950	Iodobenzene	174·3	1·25	1·6180
Mesitylene	165·2	0	1·4962	Nitrobenzene	177·2	3·94	1·5504

EXPERIMENTAL.

d-*Pinane*.—Kahlbaum's *d*-α-pinene was purified by distillation in steam in presence of a trace of sodium carbonate and was then dried and twice fractionated under atmospheric pressure. The fraction of b. p. 154·5°/757 mm. was collected; $d_{4°}^{20°}$ 0·8667, $[\alpha]_D^{20°}$ + 47·3°.

The *d*-pinene was converted into *d*-pinane by catalytic hydrogenation under pressure (cf. Lipp, *Ber.*, **1923**, **56**, 2098), the apparatus being of the type due to Adams and Voorhees ("Organic Syntheses," 1928, VIII, 10). Various preparations of platinum catalyst were tested, and the most complete absorption of hydrogen was obtained when platinum-black prepared by a modification of Loew's method (Houben–Weyl, 1928, II, 496) was used, the pinene being treated in absence of solvent under an initial pressure of 55 lb./sq. in. In this manner 97% of the theoretical quantity of hydrogen required for 23 g. of pinene was absorbed in six hours. Final purification was effected according to Lipp (*loc. cit.*), the fraction of b. p. 162—167°/758 mm. being collected and shaken with successive small quantities of a 1% solution of potassium permanganate in sodium carbonate until the colour persisted for 30 minutes. It was then distilled in steam and dried over sodium sulphate. After being distilled over sodium under diminished pressure

it was redistilled and collected at 166—166·5°/762 mm. The resulting *d*-pinane had $d_{4^\circ}^{20^\circ}$ 0·8560, $[\alpha]_D^{20^\circ}$ 22·83°, $n_D^{20^\circ}$ 1·4630 (Lipp quotes $[\alpha]_D^{20^\circ}$ 23·1° from a pinene of $[\alpha]_D^{20^\circ}$ 47·5°).

d-*Limonene*.—The original sample of limonene (B.D.H.) had a low activity and was therefore converted into the tetrabromide (Godlewsky, *Chem.-Ztg.*, 1898, **22**, 827), and the latter purified by crystallisation, giving m. p. 104°, $[\alpha]_D^{20^\circ}$ + 77·7° in chloroform (c = 7·666) (von Braun and Lemke, *Ber.*, 1923, **56**, 1562, record m. p. 104° and $[\alpha]_D^{20^\circ}$ = + 74·5° in chloroform, c = 22·4). The tetrabromide was debrominated in ethereal solution by addition of magnesium (Braun and Lemke, *loc. cit.*). Finally, the *d*-limonene was purified by being boiled over sodium and subsequently fractionated; b. p. 60·5—61°/13 mm., $d_{4^\circ}^{20^\circ}$ 0·8403, $[\alpha]_D^{20^\circ}$ 124·2° (Braun and Lemke record $[\alpha]_D^{20^\circ}$ 126·8°).

Determinations of Rotatory Power.

Concentration changes (t = 20°).

	d-Pinene in CS_2.				*d*-Pinene in C_6H_{14}.				
c	4·142 *	52·09	75·36	(Homog.)	4·038 *	20·03 †	50·06 †	70·10	(Homog.)
α_{5893}	3·39°	11·57°	17·24°	20·48°	4·08°	10·00°	24·22°	16·66°	20·48°

d-Limonene in C_6H_6.

c	2·050 *	8·128 *	42·18 *	(Homog.)
α_{5893}	4·99°	9·94°	51·95°	52·18°

* l = 2. † l = 1; in other cases l = 0·5.

Temperature changes (l = 1).

d-Pinane in nitrobenzene (c = 3·417 at 20°).

$n_D^{t^\circ}$: 1·5490 at 15·0°; 1·5468 at 20·0°; 1·5440 at 25·0°; 1·5403 at 32·0°; 1·5372 at 40·0°.

t	13·1°	18·5°	36·7°	72·6°	95·2°
$d_{4^\circ}^{t^\circ}$	1·207	1·200	1·180	1·141	1·116
α_{5893}	0·83°	0·81°	0·76°	0·69°	0·65°

d-Pinane in mesitylene (c = 1·814 at 20°).

$n_D^{t^\circ}$: 1·4969 at 15°; 1·4944 at 20·0°; 1·4923 at 25·0°; 1·4901 at 30°; 1·4877 at 35·0°; 1·4855 at 40·0°.

t	19·6°	50·5°	75·8°	96·4°
$d_{4^\circ}^{t^\circ}$	0·8665	0·8390	0·8168	0·7986
α_{5893}	0·44°	0·38°	0·35°	0·33°

d-Pinene in nitrobenzene (c = 4·068 at 20°).

t	9·1°	19·6°	48·1°	74·6°	98·1°
$d_{4^\circ}^{t^\circ}$	1·199	1·191	1·166	1·145	1·127
α_{5893}	1·15°	1·14°	1·08°	1·03°	0·98°

d-Pinene in mesitylene (c = 4·106 at 20°).

t	11·9°	20·4°	46·8°	70·5°	95·5°
$d_{4^\circ}^{t^\circ}$	0·8768	0·8699	0·8444	0·8295	0·8085
α_{5893}	1·91°	1·88°	1·85°	1·83°	1·79°

Summary.

An examination has been made of the changes in the rotatory power of optically active saturated and unsaturated hydrocarbons arising from variations in solvent, concentration, and temperature.

1. For the saturated compound *d*-pinane the rotatory powers in *non-polar* solvents vary with the refractive index of the medium in agreement with Born's expression, $M = k(n^2 + 2)^2$. Solutions in the great majority of *polar* solvents have lower rotations than the calculated values. Concentration effects in the latter cases are governed chiefly by the alteration in refractive index, but a small depression in rotatory power due to the polarity of the solvent is revealed by the influence of a rise in temperature.

2. The rotatory power of the unsaturated hydrocarbon *d*-pinene appears to be raised in strongly polar solvents and lowered in those of high refractive index. The rotation of a solution in a non-polar medium does not show a linear relationship with the degree of concentration, pinene thus behaving as a polar compound. Temperature changes for polar solvents indicate a characteristic influence due to the polarity of the solute.

3. In the case of the unsaturated hydrocarbon *d*-limonene, the rotations tend to rise in

solvents of high refractive index, but the relationship is very irregular. Concentration changes in non-polar media show that limonene has the properties of a polar compound.

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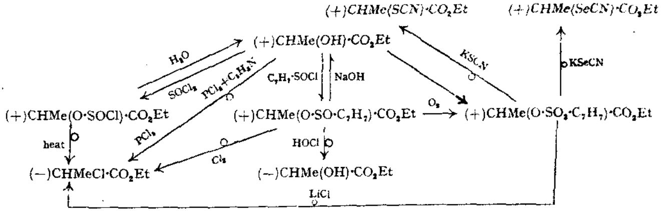
32. *The Replacement of the Hydroxyl Group of Ethyl* (+)*Lactate by Halogens, and the Molecular Dissymmetry of Derivatives of Ethyl Lactate which contain the Sulphin Group.*

By W. GERRARD, J. KENYON, and H. PHILLIPS.

A NUMBER of reactions previously used in the study of substitution at asymmetric carbon atoms in aliphatic compounds have now been applied to optically active ethyl lactate and its derivatives. The results are in harmony with, and may be interpreted in the light of, the mechanisms of these reactions put forward by Kenyon and Phillips (*Trans. Faraday Soc.*, 1930, **26**, 451). It is now shown that the (—)ethyl esters of (+)lactic, (—)α-chloropropionic, and (—)α-bromopropionic acids and the (+)ethyl esters of α-thiocyano- and α-selenocyano-propionic acids all have the same relative configuration.* Certain sulphinoxy-derivatives of ethyl lactate, to the rotatory powers of which an asymmetric sulphur atom may contribute a partial rotation, are also described.

By the interaction of phosphorus pentachloride and ethyl (—)lactate in chloroform solution, Purdie and Williamson (J., 1896, **69**, 820) prepared ethyl (+)α-chloropropionate with α_{5893} + 19·41° (or α_{5790} + 20·70°, since $\alpha_{5790}/\alpha_{5893}$ for this ester is 1·066).

It has now been found that neither the sign nor the magnitude of the rotatory power of this chloro-ester is affected when phosphorus pentachloride and ethyl (—)lactate interact in the presence of either potassium carbonate or the tertiary bases, pyridine, quinoline, and *iso*quinoline, from which it can be concluded that, even in the absence of tertiary bases, association between the reacting molecules takes place almost exclusively in the



form which leads to inversion of configuration of the asymmetric carbon atom. Similar considerations apply to the interaction of ethyl (+)lactate and phosphorus pentabromide, for, in the presence of pyridine, quinoline or *iso*quinoline, these compounds yield (—)ethyl α-bromopropionate with $\alpha^{17°}_{5790}$ — 44·1°, whereas Walker (J., 1895, **67**, 914), from the (+)ester in chloroform solution, obtained ethyl (—)α-bromopropionate with $\alpha^{17°}_{5893}$ — 43·59°. These results are illustrated in the accompanying scheme.

Ethyl (+)α-p-*toluenesulphinoxypropionate*, prepared from ethyl (+)lactate and

* The signs (+) and (—) are used in place of the terms dextrorotatory and lævorotatory; the letters *d*- and *l*- denote configurations. It is assumed that (—)lactic acid has a *d*-configuration and, in the theoretical portion of the paper, that all experiments were made with *d*-compounds. Rotatory powers are given for 1 dm. tubes.

p-toluenesulphinyl chloride in the presence of pyridine, has $\alpha_{5461}^{16^\circ}$ + 31·54°. On oxidation with potassium permanganate it is converted into ethyl (+) α-*p*-toluenesulphonoxypropionate with $\alpha_{5461}^{18.5^\circ}$ + 63·36°, a value in agreement with that recorded (Kenyon, Phillips, and Turley, J., 1925, **127**, 399) for the ester prepared by direct interaction of ethyl (+)lactate and *p*-toluenesulphonyl chloride. By distillation at low pressures, ethyl (+)α-*p*-toluenesulphinoxypropionate [from ethyl (+)lactate] can be separated into fractions of similar composition and refractive index which have rotatory powers varying from $\alpha_{5461}^{20^\circ}$ + 12·0° to $\alpha_{5461}^{20^\circ}$ + 91·4°. These variations in rotatory power must be ascribed to the separation of diastereoisomerides which arise from the asymmetry of the sulphur atom in the molecule (cf. Phillips, J., 1925, **127**, 2552).

With aqueous hypochlorous acid, ethyl (+)α-*p*-toluenesulphinoxypropionate yields ethyl (−)α-chloropropionate, with $\alpha_{5790}^{16^\circ}$ − 18·20°, and also ethyl (−)lactate, with $\alpha_{5790}^{16^\circ}$ − 9·56°. Since the (+)sulphinate has the same configuration as ethyl (+)lactate, the ethyl (−)lactate arises with inversion of configuration. With chlorine water and with bromine in chloroform solution, the (+)sulphinate yields respectively the (−)chloro- and the (−)bromo-ester. The reactions of the (+)sulphinate with hypochlorous acid and with halogens are similar in type, and it is probable therefore that these halogen esters arise with inversion and have the same configuration as ethyl (−)lactate and (+)lactic acid—see above scheme.

Similar reactions of other optically active *p*-toluenesulphinic esters have been described and discussed (Houssa, Kenyon, and Phillips, J., 1929, 1700; Houssa and Phillips, J., 1932, 1232; Kenyon, Phillips, and Shutt, J., 1935, 1663); in the present experiments the formation of the halogen derivatives is attended by less racemisation than in those previously recorded. Attempts to prepare *ethyl α-thiocyano-* and *α-selenocyano-propionate* by the interaction of ethyl (+)α-*p*-toluenesulphinoxypropionate with thiocyanogen and with triselenocyanogen were fruitless. These esters were obtained ($\alpha_{5790}^{20^\circ}$ + 15° and + 1·7° respectively), however, by the interaction of ethyl (+)α-*p*-toluenesulphonoxypropionate and potassium thiocyanate and selenocyanate respectively in alcoholic solution, reactions which may be presumed to take place with inversion of configuration (Kenyon and Phillips, *loc. cit.*; Kenyon, Phillips, and Pittman, J., 1935, 1072).

If ethyl (−)α-chloropropionate has the same configuration as (+)lactic acid, the decomposition of ethyl (+)α-chlorosulphinoxypropionate in the presence of pyridine hydrochloride is also accompanied by inversion, since Frankland and Garner (J., 1914, **105**, 1101) obtained ethyl (−)α-chloropropionate ($\alpha_{5893}^{16^\circ}$ − 3·82°) in this manner. It has been found that this (−)ester can also be obtained (*a*) with $\alpha_{5893}^{16^\circ}$ − 4·4°, by the thermal decomposition of ethyl (+)α-chlorosulphinoxypropionate alone or in the presence of pyridine, and (*b*) with $\alpha_{5790}^{15^\circ}$ − 21·74°, by interaction of ethyl (+)lactate and thionyl chloride in the presence of tertiary bases, followed by heating.

Aqueous hydrolysis of ethyl (+)α-chlorosulphinoxypropionate [from ethyl (+)lactate, $\alpha_{5893}^{16^\circ}$ + 11·30°] yields ethyl (+)lactate with $\alpha_{5893}^{16^\circ}$ + 11·02°, from which it appears that the hydrolysis does not disturb the bonds of the asymmetric carbon atom. The reaction is therefore analogous to the alcoholysis of (−)β-octyl *p*-toluenesulphinate and the saponification of carboxylic esters of optically active alcohols.

The rotatory powers ($\alpha_{5461}^{16^\circ}$ ± 380·3°) of ethyl (+)- and (−)-α-chlorosulphinoxypropionate, and also of methyl (+)α-chlorosulphinoxypropionate, $\alpha_{5461}^{15.6^\circ}$ +265·8° (Patterson and Lawson, J., 1929, 2042), are of much greater magnitude than those of other derivatives of optically active ethyl lactate. This may be due to the formation, as the result of asymmetric induction, of a second active centre in the molecule, since in the production of the chlorosulphinate a mixed sulphoxide group is introduced into a molecule which already contains a centre of asymmetry. It is not unlikely that the partial rotation contributed by such a group would be high, since the specific rotations of sulphoxides and related compounds are high (Harrison, Kenyon, and Phillips, J., 1926, 2079; Clarke, Kenyon, and Phillips, J., 1927, 188; Gajowczyk and Suszko, *Ber.*, 1935, **68**, 1005). This suggestion is strengthened by the observation that distillation of the chlorosulphinate did not result in the separation of fractions with different rotatory powers, which suggests that it contains only one of the two theoretically possible diastereoisomerides, since the distillation of ethyl

(−)α-*p*-toluenesulphinoxypropionate resulted in the partial separation of the diastereoisomeric forms.

Determination of the parachor of the chlorosulphinate provided the expected evidence that the double bond between the sulphur and the oxygen atom is semipolar in character. It appeared possible that if ethyl (+)α-chlorosulphinoxypropionate contains only one of the two possible diastereoisomerides, the interaction of this ester and *n*-amyl alcohol might give only one diastereoisomeric form of *α-carbethoxyethyl* n*-amyl sulphite* and that this would differ in rotatory power from the compound which would be obtained by the interaction of ethyl (+)lactate with *n*-amyl chlorosulphinate and may be presumed to contain two diastereoisomerides. It has been found, however, that these two methods give products which have approximately the same rotatory power and are mixtures of diastereoisomerides, since the sulphite prepared (in larger amount) from ethyl α-chlorosulphinoxypropionate could be separated by distillation into fractions of similar composition but of different rotatory power. These results do not support the view that the sulphur atom in ethyl (−)α-chlorosulphinoxypropionate has given rise to optical activity, but this may be due to racemisation at this centre of optical activity during the interaction of the chlorosulphinate and amyl alcohol. In the absence of knowledge of the optical stability during replacement reactions of the sulphur atom of sulphoxides, the possibility of an asymmetric synthesis during the formation of ethyl (−)α-chlorosulphinoxypropionate must be left undecided.

Experimental.

d(−)-Lactic acid was obtained by the method of Purdie and Walker (J., 1895, **67**, 616), and *l*(+)-lactic acid by that of Patterson and Forsyth (J., 1913, **103**, 2263). Ethyl *d*(+)-[or *l*(−)-] lactate was prepared by slow distillation during 5 hours of a mixture of *d*(−)-lactic acid (1 mol.), ethyl alcohol containing a few drops of sulphuric acid (2 mols.) and benzene (1·2 mols.). After removal of the ternary mixture (bath temp. 96°), the neutralised (calcium carbonate) ethyl *l*(+)-lactate had b. p. 54—56°/11 mm., $n_D^{16°}$ 1·4156, $\alpha_{5893}^{16°}$ + 5·70° (*l*, 0·5). The corresponding ethyl *d*(−)-lactate had $\alpha_{5893}^{18°}$ − 11·15° (*l*, 1·0). Unless otherwise stated, esters with these rotatory powers were used in the experiments described.*

Interaction of Ethyl (−)Lactate and Phosphorus Pentachloride.—(i) *In the presence of potassium carbonate.* Ethyl (−)lactate (5·9 g.) was slowly added with cooling and shaking to a mixture of dry ether (40 c.c.), phosphorus pentachloride (20·4 g., 2 mols.), and potassium carbonate (13·4 g.). The reaction product was poured into ice-water and extracted with ether; the resulting ethyl (+)α-chloropropionate (3·7 g.) had b. p. 143—144°; $\alpha_{5790}^{16°}$ + 20·86° (*l*, 1), $n_D^{16°}$ 1·4166 (Found: Cl, 25·8. Calc.: Cl, 26·0%).

(ii) *In the presence of tertiary bases.* (a) Pyridine. Ethyl (−)lactate (11·8 g.) in pyridine (7·9 g.) was slowly added to cold phosphorus pentachloride (40·8 g., 2 mols.); the mixture, after being maintained at 60° for one hour, was decomposed with ice. The resulting ethyl (+)α-chloropropionate had b. p. 144°, $\alpha_{5790}^{16°}$ + 20·93°, $n_D^{18°}$ 1·4169, $d_{4°}^{20°}$ 1·0725 (Found: Cl, 25·9%). (b) Quinoline. Similar proportions being used, the resulting ethyl (+)α-chloropropionate had b. p. 143—144°, $\alpha_{5790}^{16°}$ + 20·98°, $n_D^{16°}$ 1·4168 (Found: Cl, 25·9%). (c) *iso*Quinoline. Under analogous conditions, the resulting ethyl (+)α-chloropropionate had b. p. 143—144°, $\alpha_{5790}^{16°}$ + 20·90°, $n_D^{16°}$ 1·4167 (Found: Cl, 25·9%).

Interaction of Ethyl (−)Lactate and Phosphorus Pentabromide in the Presence of Tertiary Bases.—(a) *Pyridine.* A mixture of ethyl (−)lactate (3·54 g., 1 mol.) and pyridine (4·7 g., 2 mols.) was added to phosphorus pentabromide (13 g., 1 mol.) covered with benzene. After 3 hours at room temperature, the resulting paste was decomposed with water and yielded ethyl (+)α-bromopropionate (2 g.), b. p. 55—57°/15 mm., $\alpha_{5790}^{17°}$ + 22·05° (*l*, 0·5), $n_D^{18°}$ 1·4458, $d_{4°}^{17°}$ 1·3872.

(b) *Quinoline.* The ester (1 mol.) and base (2 mols.) yielded ethyl (+)α-bromopropionate (2·1 g.), b. p. 55—56°/15 mm., $\alpha_{5780}^{17°}$ + 22·0° (*l*, 0·5), $n_D^{16°}$ 1·4456, $d_{4°}^{17°}$ 1·3875.

(c) iso*Quinoline.* The ester (1 mol.) and base (2 mols.) yielded ethyl (+)α-bromopropionate (1·95 g.), b. p. 56—57°/17 mm., $\alpha_{5790}^{17°}$ + 22·06° (*l*, 0·5), $n_D^{19°}$ 1·4456, $d_{4°}^{16·8°}$ 1·3873 (Found: Br, 44·3. Calc.: Br, 44·2%).

*Ethyl (+)α-*p*-Toluenesulphinoxypropionate.*—A mixture of ethyl (+)lactate (25 g.), *p*-toluenesulphinyl chloride (35 g.), and pyridine (33 g.) after standing for 12 hours was poured into water, and the precipitated oil extracted with ether. The ethereal solution, after being washed with

* By calculation from data given by Wood, Such, and Scarf (J., 1923, **123**, 600), the rotation of optically pure ethyl lactate is $\alpha_{5893}^{18·9°}$ 11·65°, $\alpha_{5461}^{20°}$ 13·3° (*l*, 1).

acid and dried (potassium carbonate), yielded *ethyl* (+)α-p-*toluenesulphinoxypropionate* (60% yield), b. p. 110°/<0·1 mm., $\alpha_{5790}^{16°}$ + 12·41°, $\alpha_{5461}^{16°}$ + 14·88°, $\alpha_{4358}^{16°}$ + 24·2° (*l*, 0·25), $n_D^{16°}$ 1·5197 $d_{4°}^{16·4°}$ 1·163, $d_{4°}^{51·6°}$ 1·131 (Found, by saponification : *M*, 257·7. $C_{12}H_{16}O_4S$ requires *M*, 256).

Oxidation of Ethyl (+)α-p-*Toluenesulphinoxypropionate.*—To a stirred mixture of the sulphinate (2·56 g.) in acetone (25 c.c.) and magnesium sulphate (0·63 g.) in water (4 c.c.), potassium permanganate (0·63 g.) was added to give a permanent coloration. After addition of water and sulphur dioxide, the precipitated oil was extracted with ether, ethyl (+)α-*p*-toluenesulphonoxypropionate, b. p. 138°/<0·1 mm., $\alpha_{5461}^{19·5°}$ + 15·89° (*l*, 0·25), $n_D^{16°}$ 1·5005, being obtained. Kenyon, Phillips, and Turley (*loc. cit.*) give $\alpha_{5461}^{21°}$ + 32·2° (*l*, 0·5), $n_D^{16·5°}$ 1·5011, for the optically pure ester.

Separation of the Diastereoisomerides of Ethyl (−)α-p-dl-*Toluenesulphinoxypropionate by Fractional Distillation.*—The ester ($\alpha_{5461}^{20°}$ − 15·72°; *l*, 0·25) was thrice fractionally distilled, b. p. 110—112°/<0·1 mm., seven fractions, having the following constants, being obtained :

Fraction	1	2	3	4	5	6	7
$\alpha_{5461}^{20°}$ (*l*, 0·25)	−3·00°	3·16°	7·13°	10·51°	12·34°	19·67°	22·85°
$n_D^{20°}$	1·5165	1·5179	1·5195 *	1·5193	1·5198	1·5199 †	1·5290

* Found : C, 55·8; H, 5·8; S, 12·9 ($C_{12}H_{16}O_4S$ requires C, 56·2; H, 6·25; S, 12·5%).

† Found : C, 56·1; H, 5·9; S, 12·6%.

A second specimen of ester ($\alpha_{5461}^{16°}$ − 15·70°; *l*, 0·25; $n_D^{17°}$ 1·5198) was slowly distilled during four hours at 0·1 mm., and three fractions collected (*l*, 0·25).

Fraction.	$\alpha_{5790}^{19°}$.	$\alpha_{5461}^{19°}$.	$\alpha_{4358}^{19°}$.	$n_D^{19·5°}$.
1	−2·97°	−3·24°	−3·75°	1·5198
2	11·73	13·34	22·75	1·5199
3	18·10	20·68	—	1·5200

Reactions of Ethyl d(+)-α-p-*Toluenesulphinoxypropionate.*—(a) *With chlorine water.* Ethyl (+)α-*p*-toluenesulphinoxypropionate (5·1 g.; $\alpha_{5790}^{16°}$ + 13·35°; *l*, 0·25) was shaken for one hour with water containing the calculated amount of chlorine. After cooling, the precipitated *p*-toluenesulphonyl chloride (m. p., after crystallisation, 70°; m. p. of amide 137°) was removed by filtration from the reaction mixture, and the filtrate extracted with light petroleum. The petroleum extract contained ethyl (−)α-chloropropionate, b. p. 143—144°; $\alpha_{5790}^{16°}$ − 4·63°; $\alpha_{5461}^{16°}$ − 5·37° (*l*, 0·25) (Found : Cl, 25·85%).

(b) *With bromine.* Bromine (4·8 g.) in chloroform (20 c.c.) was added slowly to ethyl (+)α-*p*-toluenesulphinoxypropionate (7·7 g.) in chloroform (25 c.c.). After 8 days, the solution had become decolorised, and the solvent was removed at ordinary temperature. Trituration of the oily residue with light petroleum separated it into *p*-toluenesulphonyl bromide (amide, m. p. 137°) and ethyl (−)α-bromopropionate, b. p. 55—58°/15 mm., 156—157°/760 mm., $\alpha_{5790}^{16°}$ − 10·91° (*l*, 0·5); $n_D^{16°}$ 1·4463 (Found : Br, 44·32%). By the same procedure the (−)sulphinate yielded ethyl (+)α-bromopropionate, $\alpha_{5790}^{16°}$ + 8·95° (*l*, 0·5).

(c) *With hypochlorous acid.* Ethyl (+)α-*p*-toluenesulphinoxypropionate (10·25 g.; $\alpha_{5790}^{18°}$ + 63·28°; *l*, 1·0) was shaken with the calculated amount of hypochlorous acid solution ("Organic Syntheses," Vol. 5, 31) until it no longer produced a permanent coloration with starch–iodide paper. After cooling, the *p*-toluenesulphonyl chloride (m. p. 70°) was filtered off, and the filtrate extracted with light petroleum. The petroleum extract yielded an oil, b. p. 45—56°/14 mm., which, by nine fractional distillations, was separated into ethyl (−)α-chloropropionate, b. p. 42°/14 mm., $\alpha_{5790}^{16°}$ − 9·1° (*l*, 0·5), $n_D^{16°}$ 1·4166 (Found : Cl, 25·7%), and ethyl (−)lactate, b. p. 49—51°/14 mm., $\alpha_{5790}^{16°}$ − 4·78° (*l*, 0·5), $n_D^{16°}$ 1·4155 (Found, by saponification : *M*, 117·6. Calc. : *M*, 118).

(d) *With thiocyanogen.* Ethyl (−)α-*p*-toluenesulphinoxypropionate (10 g.; α_{5893} − 21·5°; *l*, 0·5) was added slowly to the calculated amount of thiocyanogen (Kaufmann, *Analyst*, 1926, 51, 157) dissolved in acetic acid. When the reaction mixture gave no coloration with starch–iodide paper, water was added, and the mixture extracted with light petroleum. The oil (4 g.) thus obtained decomposed when heated.

(e) *With triselenocyanogen.* A mixture of this compound (14 g.) and ethyl (−)α-*p*-toluenesulphinoxypropionate (10 g.) in chloroform solution was heated under reflux for several days. In this case also the oil extracted by light petroleum decomposed when distillation was attempted.

Ethyl (−)α-*Thiocyanopropionate.*—A solution of ethyl (−)α-*p*-toluenesulphonoxypropionate (8·2 g.; $\alpha_{5893}^{20°}$ − 27·5°; *l*, 0·5) and potassium thiocyanate (4 g.) in absolute alcohol (50 c.c.) was

heated under reflux for six hours, cooled, and diluted with dry ether. After removal of the precipitated potassium *p*-toluenesulphonate, the filtrate yielded *ethyl (−)α-thiocyanopropionate*, b. p. 119°/20 mm., $\alpha_{5790}^{20°}$ − 7·51° (*l*, 0·5), $n_D^{20°}$ 1·4657 (Found: C, 45·2; H, 5·7. $C_6H_9O_2NS$ requires C, 45·3; H, 5·7%).

Ethyl (−)α-Selenocyanopropionate.—A solution of ethyl (−)α-*p*-toluenesulphonoxypropionate (10 g.) and potassium selenocyanate in absolute alcohol (50 c.c.) was heated under reflux for six hours, diluted with water (300 c.c.), and extracted with ether. *Ethyl (−)α-selenocyanopropionate* was obtained, b. p. 63—64°/<0·1 mm., $\alpha_{5790}^{17·5°}$ − 0·85°, $\alpha_{5461}^{17·5°}$ − 0·91°, $\alpha_{4358}^{17·5°}$ − 1·38° (*l*, 0·5), $n_D^{17·5°}$ 1·4905 (Found: Se, 38·0. $C_6H_9O_2NSe$ requires Se, 38·3%).

Interaction of Ethyl (+)Lactate and Thionyl Chloride in the Presence of Tertiary Bases.—(i) *Pyridine*. To a cold solution of ethyl (+)lactate (4·7 g.) in pyridine (3·2 g., 1 mol.), thionyl chloride (4·8 g.) was added slowly; after being heated to 60° for one hour, the mixture was poured into ice-water, and the ethyl (−)α-chloropropionate extracted with ether. The ester (3·8 g.) had b. p. 45°/19 mm., $\alpha_{5893}^{17°}$ − 19·56°, $\alpha_{5790}^{17°}$ − 20·87°, $\alpha_{5461}^{17°}$ − 23·38°, $\alpha_{4358}^{17°}$ − 44·8° (*l*, 1·0); $n_D^{20°}$ 1·4166, $d_{4°}^{15°}$ 1·0853.

(ii) *Quinoline*. By the same procedure as in (i), but with quinoline (6·0 g.) in place of pyridine, the ethyl(−)α-chloropropionate (3·9 g.) obtained had b. p. 40·5°/12 mm., $\alpha_{5893}^{16°}$ − 19·36°, $\alpha_{5790}^{16°}$ − 20·60°, $\alpha_{5461}^{16°}$ − 23·0°, $\alpha_{4358}^{16°}$ − 44·0° (*l*, 1·0), $n_D^{20°}$ 1·4166, $d_{4°}^{15°}$ 1·0854 (Found: Cl, 25·9%); [*P*] 291·7 (Calc., from constants given by Sugden, "Parachor and Valency," 292·2).

(iii) iso*Quinoline*. Procedure as in (ii) gave ethyl (−)α-chloropropionate (3·1 g.), b. p. 40·5°/12 mm., $\alpha_{5790}^{17°}$ − 20·13°, $\alpha_{5461}^{17°}$ − 22·51° (*l*, 1·0), $n_D^{20°}$ 1·4167, $d_{4°}^{20°}$ 1·0855.

Ethyl (+)α-Chlorosulphinoxypropionate.—(i) *Preparation*. Ethyl (+)lactate (14·5 g.) was slowly added to cold thionyl chloride (22 g.) and, after the initial vigorous reaction, the mixture was heated (2 hours) on the steam-bath, then (2 hours) at 90°/15 mm., and finally distilled. Ethyl (+)α-chlorosulphinoxypropionate, b. p. 43—45°/<0·1 mm., was obtained, $\alpha_{5790}^{16°}$ + 83·0°, $\alpha_{5461}^{16°}$ + 95·08°, $\alpha_{4358}^{16°}$ + 172·4° (*l*, 0·25), $n_D^{16°}$ 1·4583, $d_{4°}^{13°}$ 1·2819; [*P*] 380·5 (Calc.: 380·4).

(ii) *Thermal decomposition*. Ethyl (+)α-chlorosulphinoxypropionate (15 g.; $\alpha_{5790}^{16°}$ + 83·94°; *l*, 0·25), distilled slowly at atmospheric pressure, gave ethyl α-chloropropionate contaminated with undecomposed chlorosulphinate which was removed by sodium carbonate solution. The ethyl (+)α-chloropropionate (7·5 g.) then had b. p. 143—145°, $\alpha_{5893}^{16°}$ − 2·2° (*l*, 0·5), $n_D^{17°}$ 1·4168.

(iii) *Interaction with pyridine*. Pyridine (15·8 g., 1 mol.) was added slowly to a cold solution of ethyl (+)α-chlorosulphinoxypropionate (40 g.; $\alpha_{5461}^{16°}$ + 190·2°; *l*, 0·5) in dry ether (50 c.c.). A white precipitate (0·4 g.) was removed, and the filtrate kept in a closed vessel. A yellow oil, which slowly turned red, was deposited, and after 2 days was separated and washed with dry ether. A portion (50 c.c.) of the combined ethereal filtrate and washings (total vol., 108 c.c.) was washed with dilute hydrochloric acid, dried (potassium carbonate) and distilled. It gave a liquid (5·5 g.) from which ethyl (−)α-chloropropionate (4 g.) was obtained, b. p. 143—144°, $\alpha_{5790}^{15°}$ − 10·87° (*l*, 0·5), $n_D^{16°}$ 1·4169, $d_{4°}^{15°}$ 1·0855 (Found: Cl, 25·8%).

The residual oil, insoluble in ether, was optically inactive in aqueous solution (Found: Cl, 14·4; SO_2, 19·0. $C_{10}H_{14}O_4NClS$ requires Cl, 12·7; SO_2, 22·9%). With picric acid in aqueous-alcoholic solution, this N-*chloropyridinium* N-*α-carbethoxyethyl sulphinate* (6 g.) gave N-*α-carbethoxyethylpyridinium picrate* (4·5 g.), needles, m. p. 95°, from acetone (Found: C, 46·9; H, 3·9; N, 13·8. $C_{16}H_{16}O_9N_4$ requires C, 47·0; H, 3·9; N, 13·8%. Cf. Gerrard, J., 1936, 688).

(iv) *Interaction with water*. Ethyl (+)α-chlorosulphinoxypropionate (8·9 g.; α_{5790} + 82·0°; *l*, 0·25) was shaken with water for 5 minutes. Extraction of the aqueous solution with ether gave ethyl (+)lactate (2 g.), b. p. 49°/12 mm., $n_D^{15°}$ 1·4155, $\alpha_{5893}^{16°}$ + 11·02° (*l*, 1·0). The ethyl (+)lactate from which the chlorosulphinate had been prepared had $\alpha_{5893}^{16°}$ + 11·3°.

(v) *Fractional distillation*. By two fractional distillations ethyl (+)α-chlorosulphinoxypropionate was divided into the following fractions, all with b. p. 43—44°/<0·1 mm. (rotations for *l* = 0·5):

Fraction	1	2	3	4	5	6
α_{5790}	+ 82·11°	+ 82·75°	+ 82·97°	+ 83·00°	+ 83·46°	+ 83·46°
α_{5461}	+ 94·16°	+ 95·05°	+ 95·16°	+ 94·95°	+ 95·96°	+ 95·96°
α_{4358}	+168·86°	+170·76°	+170·96°	+172·36°	+172·89°	+172·89°
$n_D^{19°}$	1·4584	1·4583 *	1·4583	1·4583	1·4583	1·4583 †

* Found: S, 15·85 ($C_5H_9O_4ClS$ requires S, 16·0%). † Found: S, 15·94%.

The rotatory powers of fractions 2 and 6 were unchanged after 2 weeks.

α-Carbethoxyethyl n-*Amyl Sulphite*.—(i) *From* n-*amyl chlorosulphinate and ethyl lactate*. *n*-Amyl chlorosulphinate, prepared from *n*-amyl alcohol (12·6 g.) and thionyl chloride (30 g.)

and redistilled until its refractive index became constant, had b. p. 71·5—71·75°/13 mm., $n_D^{17°}$ 1·4568, $d_{4°}^{17°}$ 1·1259, [P] 355·4 (Calc.: 354·6). It (2·1 g.) was added to ethyl (−)lactate (1·5 g.) dissolved in a mixture of pyridine and ligroin. After removal of the precipitated pyridine hydrochloride (1·46 g.), water was added, and the *α-carbethoxyethyl* n-*amyl sulphite*, b. p. 140—142°/13 mm., $\alpha_{5893}^{16°}$ − 37·15° (*l*, 0·5), $n_D^{16°}$ 1·4377 (Found: S, 12·8. $C_{10}H_{20}O_5S$ requires S, 12·7%), isolated with ether.

(ii) *From ethyl (−)α-chlorosulphinoxypropionate and* n-*amyl alcohol.* The sulphinoxypropionate (10 g.; $\alpha_{5790}^{16°}$ − 83·2°; *l*, 0·5) was added slowly to a solution of *n*-amyl alcohol (4·4 g.) and pyridine (4 g.) in ligroin (20 c.c.). After removal of pyridine hydrochloride (5·8 g.), addition of water and extraction with ether gave α-carbethoxyethyl *n*-amyl sulphite (12 g.), b. p. 140—142°/13 mm., $\alpha_{5893}^{16°}$ − 39·14° (*l*. 0·5); [P] 558·6 (Calc.: 558·2) (Found: S, 12·8%).

By two redistillations, the sulphite was separated into the following fractions:

Fraction	1	2	3	4	5	6
B. p./13 mm.	135—136°	137°	139°	143—144°	144—145°	146°
$\alpha_{5461}^{15°}$ (*l*, 0·5)	−15·12°	−18·81°	−24·31°	−30·32°	−35·70°	−48·31°
$n_D^{15°}$	1·4373	1·4375	1·4376	1·4374	1·4374	1·4376
S, %	12·81	12·85	12·81	12·85	12·77	12·72

The attempted preparation of α-carbethoxyethyl *n*-amyl sulphite by methods similar to (i) and (ii) but in the absence of pyridine gave products which could not be distilled to constancy of refractive index.

n-*Amyl sulphite*, prepared by heating thionyl chloride (5 g.) and *n*-amyl alcohol (7 g., 2 mols.) to 50° for 2 hours, had b. p. 129·5°/12 mm., $d_{4°}^{15°}$ 0·9822, $d_{4°}^{40°}$ 0·9543 (Found: S, 14·3. $C_{10}H_{22}O_3S$ requires S, 14·4%).

(+)α-Carbethoxyethyl sulphite, prepared in the same way from thionyl chloride and ethyl (+)lactate (2 mols.), has b. p. 111—112°/<0·1 mm., b. p. 161°/14 mm., $\alpha_{5790}^{15°}$ + 49·60°, $\alpha_{5461}^{15°}$ + 56·14°, $\alpha_{4358}^{15°}$ + 96·0° (*l*, 0·25), $n_D^{18°}$ 1·4402 (Found: S, 11·4. $C_{10}H_{18}O_7S$ requires S, 11·4%).

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33. *The Dipole Moments of Vapours. Part III. Homologous Series.*

By L. G. GROVES and S. SUGDEN.

IN continuation of our work on the dipole moments of vapours we have now examined the first four or five members of a number of homologous series. Our main object was to study the induction along a hydrocarbon chain, which had already been discussed for such series from measurements made on solutions (cf. Cowley and Partington, J., 1933, 1253; 1935, 604).

The values we have found for the moments are compared with those of other observers (where these are available) in Table I. In calculating the dipole moment we have taken P_A as 5% of P_E measured for the sodium line, and have recalculated the data of other workers on this basis. In some cases this brings about a considerable change. Thus Sänger, Steiger, and Gächter (*Helv. Physica Acta*, 1932, **5**, 200) find for *n*-propyl chloride $\mu = 2{\cdot}04$* from the slope of the *P–T* curve, with $P_{A+E} = 25{\cdot}3$ c.c. Since $P_E = 20{\cdot}3$ this gives the rather large value 5·0 c.c. for P_A; P_A being taken as 1·0 c.c., the value of μ becomes 2·10, which agrees well with the values we have found for the butyl and the amyl compound. Since a very small error in *P* can cause a much larger error in the slope, we think it is better in comparing the moments of a series of compounds to avoid such errors by using a definite hypothesis as to the magnitude of P_A. It will be seen from Table I that our results are in good agreement with those of other workers for methyl bromide and iodide and for a number of other substances. Some of the data in the literature, however, diverge widely from our results or those of more recent investigators; these are enclosed in parentheses in the table and are neglected in calculating the most probable value of μ given in the third column. The last column gives the difference in moment, $\Delta\mu = \mu_{RX} - \mu_{CH_3X}$.

* All moments are given in Debye units (e.s.u. × 10^{-18}).

TABLE I.

Substance.	μ, obs.	Mean μ.	$\Delta\mu$.
CH_3Cl	1·87,[5] 1·88,[6] 1·86,[3] (1·69)[1]	1·87	—
C_2H_5Cl	2·06,[5] 2·06,[6] 2·04,[3] (2·11)[1]	2·05	+0·18
n-C_3H_7Cl	2·10[8]	2·10	+0·23
n-C_4H_9Cl	2·11[8]	2·11	+0·24
n-$C_5H_{11}Cl$	2·12[8]	2·12	+0·25
CH_3Br	1·79,[3] 1·82,[1] 1·79[2]	1·80	—
C_2H_5Br	2·01,[8] 2·02,[3] (2·09),[1] (1·78)[2]	2·01	+0·21
n-C_3H_7Br	2·15,[8] 2·11,[1] (1·79)[2]	2·13	+0·33
n-C_4H_9Br	2·15[8]	2·15	+0·35
CH_3I	1·64,[8] 1·66,[1] 1·62[2]	1·64	—
C_2H_5I	1·87,[8] (2·00),[1] (1·62)[2]	1·87	+0·23
n-C_3H_7I	2·01,[8] (1·63)[2]	2·01	+0·37
n-C_4H_9I	2·08[8]	2·08	+0·44
$CH_3{\cdot}CN$	3·94,[8] 3·94[1]	3·94	—
$C_2H_5{\cdot}CN$	4·03,[8] 4·05[1]	4·04	+0·10
n-$C_3H_7{\cdot}CN$	4·05[8]	4·05	+0·11
n-$C_4H_9{\cdot}CN$	4·09[7]	4·09	+0·15
$CH_3{\cdot}NO_2$	3·54,[8] (3·48),[4] (3·78)[1]	3·54	—
$C_2H_5{\cdot}NO_2$	3·58,[8] (4·03)[1]	3·58	+0·04
n-$C_3H_7{\cdot}NO_2$	3·57[8]	3·57	+0·03
n-$C_4H_9{\cdot}NO_2$	3·55[8]	3·55	±0·01
$CH_3{\cdot}OH$	1·71,[9] 1·68[10]	1·69	—
$C_2H_5{\cdot}OH$	1·68,[9] 1·70,[10] 1·69[11]	1·69	±0·00
n-$C_3H_7{\cdot}OH$	1·64,[9] 1·66[10]	1·65	−0·04
n-$C_4H_9{\cdot}OH$	1·63,[9] 1·66[10]	1·65	−0·04

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Inspection of the figures makes it clear that the change in the moment of a compound R–X as the group R increases depends upon other factors than simple induction along the hydrocarbon chain. In the first place, it is evident that the nature of the group X plays an important part. This is well shown by the data for the alkyl halides which all have dipole moments of the same order of magnitude; if the effect is due to induction in the growing chain by a dipole of infinitely small length situated between the carbon and halogen atoms, these three series should all show much the same effect. It will be seen, however, that, whilst the chlorides show practically no increase in moment after the propyl compound, the iodides show a much larger increase in moment as the series is ascended, and a limit has not been reached at the butyl compound. The bromides show an intermediate behaviour; methyl bromide has a smaller moment than methyl chloride, whilst n-butyl bromide has a distinctly larger moment than the chloride.

Similarly, the nitro-paraffins and the nitriles, which have much larger moments than the halides, show a very small influence of the size of the radical on the dipole. With the nitro-paraffins the moment is constant from the methyl to the butyl compound within the experimental error. When comparing these compounds with the halides it must be remembered that the dipole is situated one atom further away from the growing alkyl chain, so that the Me — Et difference in the nitriles should be compared with the Et — Pr difference in the iodides. (This is true for the nitriles, but with the nitro-paraffins the C–N link which is adjacent to the growing radical has a considerable moment and should largely determine the induction.)

The theory of induction by dipoles has recently been developed by Frank (*Proc. Roy. Soc.*, **1935**, *A*, **152**, **171**) and by Higasi (*Sci. Papers Inst. Phys. Chem. Res., Tokyo*, **1936**, **28**, **284**) with special reference to the influence of solvents on the values found for moments in solution. Their conclusions can be applied to discuss the influence of the addition of non-polar groups to a polarised molecule when the moment is measured in the gaseous phase, and Frank discusses the "radical effect" in some detail.

If the molecule can be regarded as bounded by a surface of revolution about the axis of the dipole, then, by symmetry, the components of the induced moments normal to the dipole axis cancel out. The sign of the component parallel to the primary dipole depends upon the position of the polarisable part of the molecule with respect to the dipole axis. Frank shows that the induced component in any element of polarisable matter which is situated within two cones of semi-angle 55° about the axis of the dipole axis will be in the same direction as the primary dipole and will augment the measured moment. Elements situated outside these cones will have moments induced in them which will oppose the primary dipole and will diminish the measured moment. Methods of computing the magnitude of the induced dipoles are given by Frank and by Higasi; for our present purpose, however, a qualitative discussion will be sufficient.

In a homologous series it is evident that the growing carbon chain will in general, when vibrations and rotations are taken into account, add polarisable matter in a region in which the induced moment will be in the same sense as the primary dipole; an increase in moment should therefore be found on ascending any such series. Furthermore, the value of $\Delta\mu/\mu$ should be the same in all series where $\Delta\mu$ is the increase on passing from the first to the *n*th carbon atom and μ is the primary moment. It is clear from the data in Table I that the experimental values do not agree with these conclusions.

Frank (*loc. cit.*) notes that the theoretical treatment of the problem assumes (*a*) that the field distribution due to primary dipole is not altered by the introduction of polarisable matter in its vicinity, and (*b*) that the dipole is of negligible length. These approximations may not lead to serious errors in computing solvent effects but become important for the discussion of the effect of radicals on moments measured in the gaseous phase.

From the data obtained in the present investigation it appears that the polarisability of the group X plays an important part. In the methyl halides, for example, part of the halogen atom subtending an angle of more than 55° from the dipole axis is situated in a region of intense field and will be strongly polarised in a sense which will oppose the primary dipole. (This effect will be enhanced if the dipole is assumed to have a finite length or if the dipole is supposed to be embedded in the halogen atom. The dipole model is, however, but a crude approximation to the distribution of electrical charges within a molecule, so that a detailed analysis would be out of place at the present stage of our knowledge.) The addition of more CH_2 groups provides an easier path for the lines of force on the side of the molecule remote from the halogen atom, the electrical strain on the part of the halogen atom nearest the dipole will be diminished and the moment of the molecule will increase. A redistribution of the electric field as the length of the carbon chain increases can in this way produce an increase in moment along a homologous series of halides, and in particular, accounts for the order $Cl < Br < I$.

The moments found for substances in which the polar group is attached to a branched chain can also be accounted for by a redistribution of electric field. The data for some normal and branched-chain compounds are compared in Table II.

TABLE II.

Effect of Chain Branching.

Substance.	μ.	Substance.	μ.	Substance.	μ.
n-C_3H_7Cl	2·10 [6]	n-$C_3H_7 \cdot OH$	1·65 [9,10]	n-C_4H_9Br	2·15 [8]
iso-C_3H_7Cl	2·15 [8]	iso-$C_3H_7 \cdot OH$	1·63 [9]	$sec.$-C_4H_9Br	2·20 [9]
n-C_3H_7Br	2·13 [6,1]	n-$C_4H_9 \cdot OH$	1·65 [9,10]		
iso-C_3H_7Br	2·19 [9]	iso-$C_4H_9 \cdot OH$	1·60 [9]		

(For references see Table I.)

It will be seen that the halides which have the structure $\begin{matrix}C\\C\end{matrix}\!>\!CX$ possess a higher moment than the isomeric normal compounds. Branching of the chain at the carbon atom to which the polar group is attached brings more polarisable matter into the neighbourhood of the dipole and should produce a greater relaxation of the field on the halogen atom than occurs with the corresponding normal compound. On the other hand, if field redistribution is neglected, then on Frank's theory chain branching would bring part of the

alkyl group into the region in which the induced moment is zero or negative, and a small decrease in moment would be expected.

Finally, the data for some alcohols which are included in Tables I and II show a small decrease in moment on ascending a homologous series and a small decrease on passing from a normal to an *iso*-compound. The effect is not much larger than the experimental error and obviously requires further experimental study.

Experimental.

The polarisations of the vapours were measured with the apparatus described in Part I (*J.*, 1934, 1094). In the tables below, T is the absolute temperature, p the pressure of the vapour in mm. Hg, P the measured polarisation in c.c., and μ the dipole moment deduced on the assumption that P_A is 5% of P_E. All the values given for P_E refer to the Na-*D* line.

iso*Propyl chloride* (b. p. 35·5°/757 mm.; $d^{20^\circ}_{4^\circ}$ 0·8610; I.C.T. give $d^{20^\circ}_{4^\circ}$ 0·860); P_E = 20·3.

T.	p.	P.	μ.	T.	p.	P.	μ.	T.	p.	P.	μ.
288°	109	121·6	2·16	354°	184	103·1	2·16	383°	124	95·0	2·13
,,	108	122·0	2·16	,,	120	102·5	2·15	,,	186	96·4	2·15

Mean 2·15 ± 0·01.

n-*Butyl chloride* (b. p. 77·6°/748 mm.; $d^{20^\circ}_{4^\circ}$ 0·8845; I.C.T. give $d^{20^\circ}_{4^\circ}$ 0·884); P_E = 25·4.

288	54	122·4	2·11	335	77	109·7	2·12	375	73	100·2	2·11
,,	52	122·9	2·12	,,	68	108·9	2·11	,,	73	100·2	2·11

Mean 2·11 ± 0·01.

n-*Amyl chloride* (b. p. 106·3°/771 mm.; $d^{20^\circ}_{4^\circ}$ 0·8879; Karvonen, *Ann. Acad. Sci. Fenn.*, *A*, **5**, No. 6, 123, gives $d^{20^\circ}_{4^\circ}$ 0·88715); P_E = 30·3.

351	95	111·6	2·13	381	138	104·3	2·11	
,,	102	111·2	2·12	,,	110	105·2	2·13	Mean 2·12 ± 0·01.

At higher temperatures the moment suddenly increased to about 2·20—2·24. This may be due to rearrangement to *sec.*-amyl chloride.

Methyl bromide. [A commercial specimen was allowed to evaporate spontaneously at room temperature and the middle third collected and used for the measurements. During fractionation the b. p. remained steady at 4·5°/755 mm.] P_E (calc. from data for homologues) = 14·5.

291	140	83·7	1·80	335·5	130	74·2	1·79	363	165	70·0	1·79
,,	130	82·1	1·78	,,	187	73·4	1·78	,,	196	70·0	1·79
416	250	63·5	1·80	416	220	63·0	1·79		Mean 1·79 ± 0·01.		

Ethyl bromide (b. p. 38·4°/761 mm.; $d^{20^\circ}_{4^\circ}$ 1·4599; I.C.T. give $d^{20^\circ}_{4^\circ}$ 1·4602); P_E = 19·1.

292	175	106·3	2·02	346·5	195	91·6	2·00	408	210	82·6	2·03
,,	178	105·6	2·00	,,	228	91·4	2·00	,,	242	82·4	2·02
443	254	76·1	2·01	443	227	76·0	2·00		Mean 2·01 ± 0·01.		

n-*Propyl bromide* (b. p. 70·9°/761 mm.; $d^{20^\circ}_{4^\circ}$ 1·3538; Brühl, *Annalen*, 1880, **200**, 139, gives $d^{20^\circ}_{4^\circ}$ 1·3529); P_E = 23·7.

348	98	106·3	2·14	380	150	101·1	2·17	413	160	94·2	2·15
,,	160	105·3	2·13	,,	136	100·4	2·16	,,	143	92·3	2·12
441	126	90·2	2·16	441	158	89·9	2·15		Mean 2·15 ± 0·01.		

iso*Propyl bromide* (b. p. 59·3°/757 mm.; $d^{20^\circ}_{4^\circ}$ 1·315; Brühl, *loc. cit.*, gives $d^{20^\circ}_{4^\circ}$ 1·310); P_E = 24·1.

287	77	129·3	2·20	350	86	108·2	2·17	380	106	103·2	2·19
,,	85	128·7	2·19	,,	96	111·0	2·21	,,	89	101·5	2·17

Mean 2·19 ± 0·01.

n-*Butyl bromide* (b. p. 101·3°/758 mm.; $d^{20^\circ}_{4^\circ}$ 1·2745; I.C.T. give $d^{20^\circ}_{4^\circ}$ 1·275); P_E = 28·3.

352	100	109·5	2·14	378	118	104·5	2·14	413	110	98·2	2·14
,,	95	109·5	2·14	,,	110	104·9	2·15	,,	138	98·0	2·14
445	110	95·1	2·17	474	161	89·7	2·15				
,,	146	95·1	2·17	,,	186	89·9	2·15		Mean 2·15 ± 0·01.		

sec.-*Butyl bromide* (b. p. 91°/754 mm.; $d^{25^\circ}_{4^\circ}$ 1·2508; Norris, Green, and Johnson, *Amer. Chem. J.*, 1901, **26**, 308, give $d^{25^\circ}_{4^\circ}$ 1·2507); P_E = 28·4.

343	107	116·6	2·20	343	112	116·7	2·20	Mean 2·20.

When measurements were attempted at higher temperatures the substance decomposed rapidly.

tert-*Butyl bromide.* This decomposed at all temperatures at which measurements were attempted.

Methyl iodide (b. p. 42·6°/763 mm.; $d_{4^\circ}^{20^\circ}$ 2·278; interpolation from the data of Patterson, J., 1908, **93**, 1836, gives $d_{4^\circ}^{20^\circ}$ 2·2802); P_E = 1904.

T.	*p.*	*P.*	*μ.*	*T.*	*p.*	*P.*	*μ.*	*T.*	*p.*	*P.*	*μ.*
295	164	76·8	1·64	337	174	69·5	1·64				
,,	157	76·6	1·64	,,	157	69·5	1·64		Mean 1·64 ± 0·01.		

Ethyl iodide (b. p. 72·0°/758 mm.; $d_{4^\circ}^{20^\circ}$ 1·934; from data of Tyrer, J., 1914, **105**, 2534, $d_{4^\circ}^{20^\circ}$ = 1·9355); P_E = 24·3.

293	96	98·3	1·86	293	103	99·9	1·88	293	89	99·4	1·87
337	105	88·7	1·86	337	100	90·4	1·88	337	75	89·7	1·88
					Mean 1·87 ± 0·01.						

n-*Propyl iodide* (b. p. 102·4°/760 mm.; $d_{4^\circ}^{20^\circ}$ 1·7428; Brühl, *Annalen*, 1880, **203**, 15, gives $d_{4^\circ}^{20^\circ}$ 1·7427); P_E = 28·9.

337	97	104·7	2·01	337	97	104·4	2·01	337	74	104·6	2·01
374	127	97·4	2·01	374	100	97·6	2·02	374	126	97·7	2·02
					Mean 2·01 ± 0·01.						

n-*Butyl iodide* (b. p. 129·6°/760 mm.; $d_{4^\circ}^{20^\circ}$ 1·616; Brühl, *loc. cit.*, gives $d_{4^\circ}^{20^\circ}$ 1·6166); P_E = **33·5**.

349	96	111·9	2·08	415	136	98·9	2·07	415	153	99·4	2·08
349	104	111·9	2·08	415	126	98·9	2·07		Mean 2·08 ± 0·01.		

Acetonitrile (b. p. 81·4°/758 mm.; $d_{4^\circ}^{20^\circ}$ 0·7822; I.C.T. give $d_{4^\circ}^{20^\circ}$ 0·7824); P_E = 11·1.

354	66	283·3	3·95	404	74	247·2	3·93	433	89	233·0	3·94
,,	68	280·7	3·93	,,	90	247·2	3·93	,,	77	232·2	3·93
463	96	218·2	3·94	463	103	217·9	3·93		Mean 3·94 ± 0·01.		

Propionitrile (b. p. 97·1°/759 mm.; $d_{4^\circ}^{20^\circ}$ 0·7822; I.C.T. give $d_{4^\circ}^{20^\circ}$ 0·7824); P_E = 15·8.

351	56	302·0	4·03	408	73	262·1	4·03	443	115	242·5	4·03
,,	67	302·6	4·03	,,	76	263·9	4·04	,,	67	241·0	4·01
469	56	231·8	4·05	469	132	230·6	4·03		Mean 4·03 ± 0·01.		

n-*Butyronitrile* (b. p. 116·6°/755 mm.; $d_{4^\circ}^{20^\circ}$ 0·7914; I.C.T. give $d_{4^\circ}^{20^\circ}$ 0·7909); P_E = 21·2.

339	57	321·4	4·06	375	68	289·5	4·04	407	82	269·0	4·04
,,	55	321·4	4·06	,,	70	289·8	4·04	,,	88	272·3	4·07
443	91	248·3	4·04	443	117	248·4	4·04		Mean 4·05 ± 0·01.		

Nitromethane. We are indebted to Dr. D. J. G. Ives for one specimen of this compound which had been purified for conductivity work. It had b. p. 99·1°/758 mm.; $d_{4^\circ}^{25^\circ}$ 1·1311. Wright, Murray-Rust, and Hartley (J., 1931, 199) give $d_{4^\circ}^{25^\circ}$ 1·1312. Since our results for this substance differed from those of Smyth and McAlpine (*loc. cit.*), another specimen was purified by us and had $d_{4^\circ}^{25^\circ}$ 1·1312. The measurements made with the second specimen are marked with an asterisk below. It will be seen that the two specimens gave almost identical moments. P_E = 12·5.

337	73	244·7	3·56	367	65	223·5	3·54	416	72	198·6	3·54*
,,	62	243·5	3·55	,,	89	227·1	3·57	,,	90	197·9	3·53*
416	93	200·9	3·56*	453	96	182·1	3·52*	454	108	183·7	3·54
453	100	182·6	3·53*	454	80	182·9	3·54		Mean 3·54 ± 0·01.		

Nitroethane (b. p. 113·1°/738 mm.; $d_{4^\circ}^{24·3^\circ}$ 1·0469; $n_D^{24·3^\circ}$ 1·3901; Brühl, *Z. physikal. Chem.*, 1895, **16**, 193, gives $d_{4^\circ}^{24·3^\circ}$ 1·0472); P_E = 17·0.

365	65	232·5	3·56	389	82	220·9	3·58	428·0	107	201·9	3·57
,,	62	233·8	3·57	,,	90	220·6	3·57	,,	102	202·3	3·58
461	96	191·9	3·61	461	135	188·1	3·57		Mean 3·58 ± 0·01.		

α-*Nitropropane* [b. p. 131·4°/766 mm.; $d_{4^\circ}^{24·3^\circ}$ 0·9974. This is lower than the value given by Brühl (*loc. cit.*), *viz.*, $d_{4^\circ}^{24·3^\circ}$ 1·0081. Perkin (J., 1885, **46**, 688) gives $d_{25^\circ}^{25^\circ}$ 1·0023, whence $d_{4^\circ}^{25^\circ}$ 0·9994]; P_E = 21·4.

343	58	253·0	3·58	388	98	225·3	3·57	423	108	207·4	3·56
,,	60	252·6	3·58	,,	90	224·2	3·56	,,	117	207·2	3·56
466	107	193·0	3·59	466	143	189·8	3·56		Mean 3·57 ± 0·01.		

α-*Nitrobutane* (b. p. 151·8°/763 mm.; $d_{4^\circ}^{25^\circ}$ 0·9685; n_D 1·4078); P_E = 26·2.

373	79	238·4	3·57	416	72	214·0	3·55	441	88	204·5	3·56
,,	64	237·5	3·56	,,	97	213·3	3·54	,,	130	205·4	3·57
470	107	192·4	3·54	470	121	192·2	3·54		Mean 3·55 ± 0·01.		

We are indebted to Dr. J. J. Fox, O.B.E., for giving us facilities for carrying out this work.

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Pigments, Mediums, and Technical Methods of Classical and Mediæval Painters.

A LECTURE DELIVERED BEFORE THE CHEMICAL SOCIETY ON OCTOBER 29th, 1936.

By A. P. LAURIE, M.A., D.Sc.

THE subject covered by this title is of vast extent and to give all the sources of information and all the experiments made by myself and others would fill a stout volume. I therefore propose to confine myself to giving results and conclusions and only to deal with sources of information and experimental reasons for certain conclusions at such points as are still open to question or are of especial interest.

To begin with the pigments used in classical times, we have two valuable sources of information, Pliny and Vitruvius, and further we have been able to analyse the pigments found at Pompeii and on the Egyptian paintings. It is evident that at the time when Pliny wrote, a large number of pigments were available for the painter. There were what the artist calls the "earth colours," the red and yellow ochres and terra verte, and the blue and the green carbonate of copper, azurite and malachite, also cinnabar and orpiment, and chalk for a white pigment. In addition to these natural pigments, the two oxides of lead were known, massicot and red lead, and Pliny describes the manufacture of white lead by what was practically the stack process of to-day, and the manufacture of verdigris by the corrosion of copper plates buried in the grape skins from the wine vats. He also describes the precipitation of dyes by means of alum and lye from wood ashes, and tells us that a blue pigment can be obtained from woad and the indigo dye vats, and a pigment derived from the *Murex* shell fish by absorbing the dye in a white earth used for cleaning silver. This may have been an infusorial earth. Although the preparation of mercury from its ores was known, there is no mention of the making of vermilion, which is first described in the Lucca MS., 8th century. For black there were, of course, carbon blacks from charcoal, and lampblack.

In addition the ancients had the blue pigment, made in Egypt, which has been the subject of so much investigation. This blue is a calcium copper silicate which does not occur in nature and is made by an interesting process. Sand is mixed with copper carbonate, lime and a little soda, and kept at a temperature between 800° and 900° for about 24 hours. The whole mass forms a frit in which the crystals of the calcium copper silicate are slowly formed, and the crystals are afterwards separated by grinding and washing. The soda seems to act as a carrier. Below 800° the blue is not formed and above 900° a green glass is obtained, so the temperature has to be carefully regulated for days.* The blue dates from the 6th dynasty and is found on the frescoes at Knossos, and was the universal blue used at the time of Pliny. Somewhere between the second and the seventh century of our era the secret was lost. The furnaces containing cakes of blue have been found buried in the sand of Egypt, and the only known recipe is given by Vitruvius. Until the time of the Ptolemies the Egyptian palette was very limited: carbon black, chalk, red and yellow ochre, Egyptian blue, the green formed by overheating the blue, and malachite.

Although, owing to the uncertainty of the nomenclature, it is impossible to be sure, the production of ultramarine from lapis lazuli does not seem to have been known, though lapis lazuli itself was used as a precious stone. For mediums they had gum acacia, glue, and beeswax. White of egg was used to attach gold leaf, and white or yolk of egg, or a mixture, may have been used as a painting medium, though we have no direct evidence on this point. The use of the drying oils as varnishes or as painting mediums seems to have been unknown. One group of painters used nothing but beeswax, mixed with pigment, either modelling the beeswax with hot bronze tools, or laying on the melted wax, mixed with the pigment, with a brush. Examples of these wax paintings have been found at Hawara in Egypt, in which both methods were used.

As much purely speculative writing on this subject of wax painting is based on the assumption that to paint with pigment mixed with melted wax was impossible, I studied

* *Proc. Roy. Soc.*, 1914, *A*, **89**, 418.

the technique with the assistance of some art students, and we produced pictures which could not be distinguished in appearance from oil paintings.* The difficulty in this climate is due to the rapid cooling of the wax on the surface of the picture. The panel or canvas must be kept warm. As Flinders Petrie has pointed out, in the climate of Egypt the difficulty was the other way, the wax remaining liquid too long.

Wax was also used as a protective medium. The wall paintings in Pompeii were probably done as follows. Layer upon layer of plaster was laid on the walls, each coat before the last was quite dry. The final coat was composed of lime and marble dust, sometimes mixed with pigment, and was brought to a polished surface with the plasterer's trowel. The painting on this surface was probably done with pigment mixed with a little lime or lime water. I have found that a skilled plasterer can produce a surface like polished marble in this way, and that owing to the mass of damp plaster pigments laid on after 24 hours firmly adhere, the painting on plaster freshly laid not being necessary. Finally in some cases wax was driven in by hot braziers. There is no evidence that lime soaps were used as some writers have supposed.

When investigating ancient crafts, we must strictly observe two rules. We must not assume a material or process which is not either found or described, and we must not forget that skill in craftsmanship overcomes the difficulties due to the simplicity of the material.

We have no record of the medium used by the second group of painters whom Pliny mentions.

Turning from Rome and the Roman Empire to Byzantium from the 7th century, we find on illuminated MSS. a red, probably very pure cinnabar, orpiment, malachite, ultramarine from lapis lazuli, and a beautiful crimson pigment probably prepared from *Murex*. Egyptian blue has disappeared. In the Scoto-Irish monasteries, mercury sulphide is replaced by red lead in the earlier MSS. and a pigment prepared from the local shell fish *Purpura capillus*, which is more purple than the pigment from the *Murex*.

A differentiation soon appears in the colour scheme and pigments used on European MSS. on the one hand, and on the Scoto-Irish and Byzantine MSS. on the other. The *Murex* pigment soon disappears from European MSS. and is replaced by a lake corresponding closely to what we call crimson lake. This may have been derived from Brazil wood, kermes or similar cochineal insects, or lac. The recipes for these lakes are very old and I have prepared them all. They are very similar in tint. The lake from kermes is the fastest to light, and Brazil wood lake the most fugitive, but none of them compares in permanence with madder, for which no recipe is given till the 17th century, except an old Egyptian recipe for heating madder root with lime and gypsum, which produces a dull red pigment.

The ultramarine in the early MSS. was very crudely separated from the other minerals in lapis lazuli and while a gradual improvement is seen in the ultramarine on European MSS. the crudely prepared ultramarine was used up to the 12th century on Scoto-Irish MSS., and up to the conquest of Byzantium by the Turks on Byzantine MSS. In fact the palette remained unaltered. The persistence of this older tradition in Irish and Scottish monasteries raises interesting questions as to the origin of Christianity in these Islands and on trade routes.

I cannot leave this early period before 1200 without mentioning two interesting facts. Gold leaf and gold leaf ground as a pigment were of course known from very early times, but on some English MSS. from the 9th to the 10th century I found that gold dust, evidently from river-washed gold, had been used.

Perfectly prepared ultramarine is first found about 1200, and the recipe for its preparation given by Cennino Cennini and other writers is very interesting in the light of our modern methods of ore separation, and the study of emulsions and of surface tension. The finely ground lapis lazuli was mixed with Venice turpentine, a resin, and beeswax, and kneaded from time to time with fingers wet with linseed oil. After some days the mixture was placed in warm water containing a little lye from wood ashes, and kneaded with wooden pestles. The ultramarine separated, leaving the other minerals behind.

* "Greek and Roman Methods of Painting," Camb. Univ. Press.

The cheap blue pigment was apparently always azurite, but deposits were occasionally found so fine in colour that they rivalled ultramarine. The use of azurite occurs on certain illuminated MSS. between 1250 and 1400, and again later. Evidently a very beautiful deposit of azurite was found about 1480, and continued in use to about 1640, when it disappeared from the artist's palette. De Wilde has found it as late as 1660 on one picture only (" The Scientific Examination of Pictures," Martin de Wilde). It was stated to come from Hungary.

The first undoubted example of a madder lake I have identified in the " Speculum Vitae Christi " (18.1.7. Adv. Lib. Edin.), a MS. in the Advocates' Library, Edinburgh, painted between 1460 and 1490. This MS. is also remarkable for having been largely painted with a wax medium, which must have been dissolved in some volatile solvent like oil of turpentine : this therefore is the earliest definite evidence of the use of turpentine as an artist's medium.

Smalt blue first appears about 1600, and the artificial basic carbonates of copper, the blues and greens known as blue and green bice, about 1610—1620, ultimately replacing azurite.

Multitudinous recipes exist for the preparation of blue, green, red, and yellow pigments from vegetable dyes, and from copper. For these I must refer you to Mr. Daniel Thompson's book, " The Materials of Mediæval Painting." Prussian blue appears in the 18th century.

Before leaving the subject of pigments, it is of interest to note that, apart from lakes prepared from dyes, which have only proved permanent in illuminated MSS., the mediæval paint box consisted of minerals; pigments made at a comparatively high temperature, massicot, red lead, Naples yellow (antimony and lead oxide), vermilion; and pigments made by a slow process of corrosion, white lead, and verdigris. These pigments, with the possible exception of red lead, though many of them are quickly destroyed or discoloured by chemical reagents, have proved remarkably permanent throughout the ages. Even verdigris, which has been condemned, is, I believe, more reliable than is supposed. The copper pigments have been condemned for two reasons : being transparent and of poor staining power, they are affected by the yellowing of oil and varnish, and they have been in many instances blackened by the use of alkali and strongly alkaline soaps by restorers. The verdigris used mixed with ultramarine in Watteau's blues is in perfect condition, and the brightest green on a canvas on which oil paints have been painted out, some forty years old, is verdigris. I found on a German MS. of the 11th century (Laing, 5 Ed. Un. Lib.) a copper green which I identified as a copper resinate. The earliest known recipe for such a green is in the De Mayerne MS. (Sloan MS. 2052).

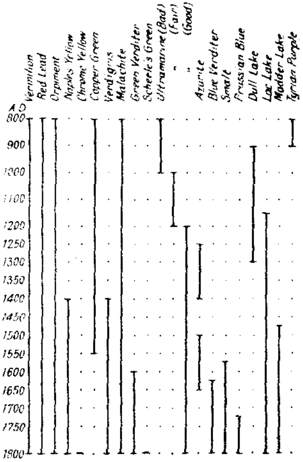


FIG. 1.

Graph showing dates when certain pigments came in and went out.

The yellow lakes used by the Dutch painters have faded, and the red lakes have turned brown and faded, but laid thinly on a bright red background have preserved the richness of colour with which we are familiar.*

* " The Pigments and Mediums of the Old Masters," Macmillan.

Mediums.

Yolk of egg replaces wax as a medium on the Greek ikons after the 6th century,* and is the Italian 13th, 14th, and 15th century medium, being superseded by oil towards the end of the 15th century. It has proved remarkably permanent, retaining its firmness and the freshness of the pigments and resisting organic solvents. We fortunately possess in the book of Cennino Cennini of about 1400 a detailed account of both how to paint in this medium and how to paint in fresco.

The use of drying oils as a medium is described by Theophilus in the 12th century, and the account books of Ely and Westminster of the 13th and 14th centuries show they were the principal medium used in England at that time. Linseed oil, hempseed oil, walnut oil more especially in Italy, and, in the 17th century, poppy oil were used.

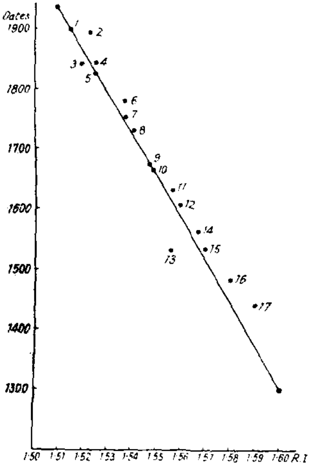


Fig. 2.

We now come to a very interesting question, namely, the technical methods and the medium of the northern 15th-century painters. We have unfortunately no authoritative detailed account of their methods, pigments, and mediums like the book of Cennino Cennini on tempera painting, and must try and arrive at as much knowledge as we can by examination, experiment, and such information as we possess.

There are two problems before us—the extraordinary brilliancy and state of preservation of the early oil paintings, and certain peculiarities of brushwork and technique that continue to the time of Rubens and are more or less present in the Dutch little masters, including Vermeer. Before discussing these problems it is necessary to mention a property of the solid film of the drying oil.

In 1925 a committee consisting of painters and chemists was set up by the Royal Academy to investigate the problems of the modern painter and of the curator. Having no funds for experimental work, it had a short life, but owing to the voluntary work of the chemists on it a little pamphlet was published containing much valuable information which is buried in the archives of the Royal Academy.

One thing had impressed me about modern oil painting and that was the rapid lowering in tone of oil pictures. If a little chrome yellow in oil is spread out and allowed to dry, the dried pigment is already duller and more orange than the pigment in the tube. I asked my friend Dr. Morrell whether it was not possible that the dry linseed oil film kept rising in refractive index as it got older, thus making pigments ground in it more translucent. As no one seemed to know, I bought a refractometer and spread on it a film of linseed oil, which is now ten years old and has never been disturbed. The refractive index rose rapidly at first, then more and more slowly, but is still rising and is to-day 1·512.

Rise in the Refractive Index of the Linseed Oil Film on the Herbert Smith Refractometer.

Days.........	—	1	3	5	8	31	260	865	2700	3885
R.I.	1·480	1·482	1·486	1·492	1·494	1·495	1·500	1·505	1·510	1·512

It is only necessary to examine pigments in liquids of high refractive index to realise how important this is to the oil painter. White lead becomes grey and translucent, and

* I have found on an ikon of about 1700, probably from the Caucasus, a ground of beeswax and yellow ochre, on which the painting was done with beeswax and a drying oil. This revival of an old technique may have been due to the restoration of Christianity in Tiflis at about this time.

FIG. 3

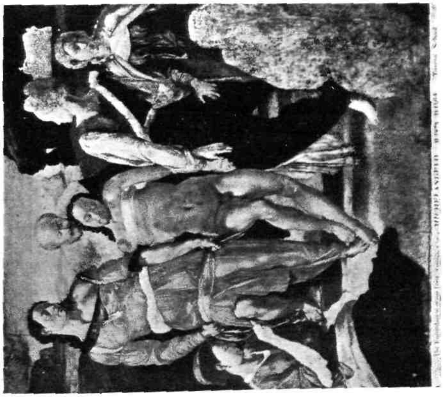


FIG. 5.

FIG. 4.

FIG. 6

cadmium yellow and chrome yellow become orange and dull. It seemed of interest to push this matter further and, as many pictures are sent to me to examine, I took to measuring the refractive index of the film of oil by taking a minute sample of the white lead paint, dissolving out the white lead, and measuring the refractive index by an immersion method. I was fortunate early in my experiments to be asked to report on the genuineness of a painted stone statue of 1300, which gave me a starting point of 1·600 R.I. I am publishing the details of these experiments elsewhere.

You will see from Fig. 2 that with occasional irregularities the refractive index of the oil film in old pictures increases with age with marked regularity. Doubtless further researches may reveal exceptions and irregularities, but the general proposition is demonstrated and it accounts among other things for the pentimenti in pictures, and gives us a fresh insight into the technical methods of the early painters in oil.

It is well known that when one oil painting is made over another one, the underpainting ultimately shows through. An interesting example is the appearance of the floor tiles through the dress of the woman standing by the fireplace in the picture by Pieter de Hooch (Nat. Gal. No. 834) (Fig. 3). This increase in translucency must be taking place over the whole surface of oil paintings all the time.

We have enough unfinished pictures of the 15th and early 16th centuries to understand their method. Starting with a surface of gesso, either of gilder's whitening or plaster of Paris which had been mixed with a large volume of water, and glue, the picture was drawn, and either painted in tempera in black, with the gesso for white, or in colour in a tempera medium. On this unchangeable brilliant opaque foundation (egg does not change in refractive index with age) a thin painting of oil colours was laid. As the oil rose in refractive index with age, it became more translucent, and colour and light penetrated more freely through the oil film. Fugitive pigments, such as lakes which fade to a brown, retained their value from the red light reflected from the underpainting. In this way the rise in refractive index of the oil counteracted the dulling caused by yellowing of the oil and fading of pigments.

The unfinished picture by Jan Van Eyck, "The Santa Barbara," in the Antwerp Gallery has been entirely drawn in in black white, and in one corner the blue sky has been laid in in oil (Fig. 4). We have in the Edinburgh National Gallery an unfinished picture, attributed to Cima da Conegliano, complete in tempera, with the oil painting begun on the sky and on the Virgin, and in the National Gallery there are two unfinished pictures by Michelangelo, in which the tempera underpainting has been carried out (Nat. Gal. 790, 809). In 790 the robe of one figure has been laid in in red, ready for the final glazing in oil (Fig. 5).

When this elaborate method was abandoned, the painting was still done on a white priming and the high lights were very thinly painted. Later on, though white lead, very dry and with the minimum of oil, was lumped on for a high light, thin painting on a white ground was continued. To Rubens is attributed the reverse policy, thick painting for high lights and thin painting in the shadows, and Rembrandt reversed the whole technique, but he began on a white ground, on which he thinly scumbled a brown pigment.

It is only necessary to walk quickly through a series of rooms containing pictures of the 15th, 16th, 17th, and 18th centuries to realise that these get darker and lower in tone. Studio tradition had resulted in the sound methods of the 15th-century painters, but of course the scientific reasons were not understood and so it was gradually abandoned. An interesting example of its use is the Rokeby Venus. The background is on a red ochre priming laid over white lead, the Venus on a white priming.

But this is not the whole of the story. There are certain qualities in the paint surface and brushwork of the early painters that cannot be reproduced by raw linseed oil paint, and have led some painters to make the assumption, for which there is no historical evidence, that some kind of emulsion was used. Eastlake sought the solution in the assumption that an oleo-resinous varnish was used. A little varnish was occasionally added to the pigment ground in oil, but there is no evidence of painting entirely in varnish.

Together with the custodian of the gallery in Vienna I was looking the other day at some pictures painted by Rubens himself. We agreed that his medium had qualities

which are not possessed by raw oil paint. It was the custodian of the gallery in Edinburgh who challenged me to paint the signature in the Arnolfini picture by Van Eyck in the National Gallery in oil paint: his challenge induced me to take up the question afresh and study again the old recipes. A great deal of attention has been devoted of late years to the study of the polymerisation or condensation products obtained by heating linseed oil, which are known as stand oils. These thickened oils have long been made in Holland, and were used, when prepared by a slightly modified process, for making printer's ink. When used to paint with, they leave a perfectly sharp edge, yet within that edge they flow to form a smooth polished enamel surface. They are remarkably durable, and white lead ground in stand oil remains white while white lead ground in raw oil rapidly becomes yellow. The objection to the theory that they were used by the early oil painters is that they form a sticky medium which, unless thinned with turpentine, no modern painter could use, and the evidence is that turpentine was not used as a medium in the days of Van Eyck.

It seemed nevertheless advisable to look again into the old recipes for preparing linseed oil for painting. To begin with the famous account given by Vasari of what he calls the invention of Van Eyck, he tells us that pigments are ground in walnut or linseed oil, which is their medium, thus disposing of the idea that emulsions and other complex mixtures with wax were used in painting. He also says that Van Eyck *boiled* the oil with certain admixtures of his and that the oil gave a *gloss* of itself without varnish. This might mean the preparation of a stand oil or a drying oil, with litharge, but at any rate the oil was not used raw.

The oldest recipe we have for preparing oils for painting is in the MS. of Eraclius, probably of the 13th century. The oil with the addition of a little lime is to be heated and continually skimmed. When cold it is mixed with white lead and put in the sun for a month or more and frequently stirred. A thickened oil made by this process contains a lime soap. During exposure to the sun an appreciable quantity of white lead is dissolved to form lead soap (Merrifield, Vol. I, p. 232). We thus have a stand oil in which a certain amount of a lead dryer has been introduced by a subsequent process.

The next recipe I shall refer to is the Strasbourg MS. A.VI. No. 19, Public Library, Strasbourg (Eastlake, Vol. I, p. 130). There linseed, hempseed, or old nut oil is to be boiled with skimming with the addition of old bones and pumice stone. I find that, on boiling with bone ash, some 3% of a lime soap is dissolved in the oil. Whether the introduction of lime soap in these oils has any significance is worthy of enquiry. The cold oil is clarified by stirring it with anhydrous zinc sulphate and strained. The author of the recipe says: "The oil will acquire a thick consistence." In this oil pigments are to be ground, and finally a few drops of varnish are to be added.

Messrs. Pearson, who manufacture stand oils, have carried out some interesting experiments on oils boiled in open copper vessels and in copper vessels with a narrow neck. The open vessel gives a stand oil suitable for the painter, the vessel with the narrow neck a stand oil suitable for printing ink. It is to be noted that the development of oil painting and printing went side by side and doubtless the same oil merchants prepared both oils.

Note. Cennino Cennini gives two methods of preparing oil. To make a medium for attaching gold leaf, he boils the oil till reduced to half its volume, and he prepares it for painting by exposing it in a copper bowl till "reduced to half its volume." I have pointed out that the volume would not be reduced in this way, and that the Italian is capable of meaning "till it is bleached." Mr. Daniel Thompson has made a better suggestion, namely, that the oil exposed to the air becomes covered with a thick skin which reduces the volume of liquid oil. A pure cold-pressed linseed oil exposed in an open vessel to sun and air forms a thick skin, and the oil below is very viscous, does not yellow so badly as raw linseed oil, and though not so good as stand oil, has similar properties as a medium. It is possible this was used in Italy. It is interesting to note that this polymerised oil dissolves completely in acetone, thus showing a different polymerisation from that produced by heat.

The question still remains, can a picture be painted with a pigment ground in stand oil? In order to answer it I went to the sign painters, who carry on the old traditions. The

sign painter uses a soft brush and a sticky medium. He soaks the oil out of ordinary artists colours with blotting paper and mixes them with a little varnish like those prepared for gilding. He requires a sticky medium to hold the brush. I gave a clever young sign painter some stand oil and a full-sized photograph of the Van Eyck signature and told him to grind lamp black in the oil and copy the signature. The very perfect copy produced shows that it can be reproduced in stand oil (Fig. 6). Stand oil as a medium had exactly the properties he wanted and he was very much interested in Van Eyck's brushwork, recognising in it the qualities that he could get with stand oil alone.

Later on, with the introduction of turpentine towards the end of the 15th century, the use of a stand oil medium became easy. The probability is that artists did not attempt to prepare their own oil, and that, as the demand grew for a freer and more facile handling of oil paint, the oil merchant passed from stand oil to stand oil and raw oil mixtures, very likely adjusted to suit the needs of the painter (Vermeer certainly used a good deal of stand oil), until raw oil alone was used to give the artist the slick medium of to-day which has been the ruin of the permanency of oil painting. The peculiar qualities of surface and brushwork and the remarkable durability of the early oil paintings can be attributed to the method by which the picture was built up on an underpainting upon a white gesso of tempera painting and to the use of the thickened polymerised oils, known as stand oils, in which the pigments were ground.

I have made no attempt here to describe the technical methods required in investigations in which the material is limited to one or two minute particles removed from a picture. For the removal of a particle, either an ordinary hypodermic needle can be used, or a hypodermic needle cut across and ground so as to make a minute cork borer by which a sample is removed, giving a cylinder of paint right through a picture which can be mounted in paraffin wax and cut in sections.

The well-known methods of micro-analysis are available for the identification of pigments, but require modification where only one or two minute and possibly very insoluble particles are available. One method I have found very useful is to dissolve the particle in a small borax bead. Layer after layer can be dissolved off the bead, placed on a glass slide, by successive drops of water, and a separate test applied to each residue (*The Analyst*, 1934, **59**, 246).

OBITUARY NOTICES.

PAUL BORG.

1888—1936.

PAUL BORG was born in Malta on November 30th, 1888. He matriculated in the Malta University in 1906, and attended the academical course of science for the next three years. In 1909 he qualified as chemist and pharmacist; subsequently he applied himself to the study of chemistry, entomology, and plant pathology, and succeeded in elucidating numerous obscure points in the life history of insect pests and fungous diseases. In 1919 he published an illustrated booklet on "The Scale-insects of the Maltese Islands," giving also in detail the various methods of treatment.

In 1920 Borg was appointed plant pathologist to the Department of Agriculture, and at once started an extensive campaign for the reconstitution of vineyards destroyed by the *Phylloxera*, for the establishment of nurseries of American vines, with a view to providing ample supplies of suitable stock for grafting, and for the treatment of insect pests and plant diseases, particularly scale-insects, woolly aphis, fruit-tree borers, and the fruit-fly, and the fungous diseases of the vine and the potato.

In 1921, at the suggestion of Lord Blyth, and under the auspices of the Colonial Research Committee, Borg was entrusted with an investigation into the wine-making processes obtaining in Portugal (the districts of Estremadura and the Alto Douro), in Spain (Jerez de la Frontera, Malaga, Barcelona, Reus, and Villafranca), in France (the region of Bordeaux), and in Algiers and Tunis. The object was primarily the study of the liqueur wines as produced in Spain and Portugal, and of the table wines of Bordeaux. The tour of inspection lasted four months, and on his return to Malta, Borg collected the various reports which he had submitted to Lord Blyth, and published at the Government Press his "Report on a Tour of Inspection in the Wine-growing Districts of Western Europe and Algeria," teeming with valuable information and conveying an insight into trade secrets, particularly in the production of the superior brands of sherry.

Borg, who was apparently in good health, succumbed to a sudden attack of angina pectoris, early in the morning of May 7th, 1936.

J. BORG.

THOMAS ELLISS CLARKE.

1914—1936.

CLARKE was born in Manchester on August 23rd, 1914. The North Manchester Municipal High School was inaugurated in 1926, and he was one of its first pupils. He matriculated in the Northern Universities in 1930, and obtained their Higher School Certificate in 1932. He was offered, but did not take up, a scholarship at the Manchester College of Technology, preferring rather to come to London and study for the teaching profession. He accordingly entered King's College in the autumn of that year, with the assured prospect of a session at the Institute of Education subsequent to his undergraduate course. Originally he had meant to study physics and, at the conclusion of his Intermediate Science year, any of the Departments of Mathematics, Physics, and Chemistry would gladly have accepted him as a student. He actually decided on chemistry, and during the next two years it became evident that chemical industry would have been the career of his choice if he had been a free agent. He graduated with Honours in 1935 and, after a certain degree of hesitation, decided to proceed with his Teachers' Diploma course, as was normal for a man in his position. At first, he attempted to combine with this work research in physical chemistry at the Battersea Polytechnic, but was compelled to stop the latter, as being deemed inconsistent with his education studies. He was taken ill in July, 1936, and died early in August.

Clarke was a man of solid character, with good physical presence, a diffident and rather charming personal manner, an essentially sane and balanced mind, and a generous and

attractive nature. He won golden opinions during his schooldays, and his headmaster had always hoped that he would return to the school as a member of the staff. Indeed, he had in high measure those qualities which go to make a good schoolmaster, qualities which made him much appreciated during his college career, at the Institute of Education and at St. Paul's School, where he carried out his teaching practice. He inspired in his friends an unusually warm attachment, and all who knew him regret the tragic end to his brief career.

A. J. ALLMAND.

VICTOR GRIGNARD.

1871—1935.

FRANÇOIS AUGUSTE VICTOR GRIGNARD, who was elected to the Honorary Fellowship of our Society in 1920, was the son of Théophile Henri Grignard, a sail maker of Cherbourg. After receiving his early education at Cherbourg and Cluny, he entered at the University of Lyons and secured his licentiate in due course. At first, Grignard proposed to specialise in mathematics, but, inspired by Bouveault, then a junior lecturer in chemistry at Lyons, he decided to specialise in organic chemistry.

Grignard's first investigations were carried out in 1898 and 1899 and described in three short papers on "ethyl β-*iso*propylacetobutyrate and the stereoisomeric di*iso*propylbutenedicarboxylic acids" (with Barbier), "a new sexavalent hydrocarbon: 2-methyl-3-hexene-5-ine," and "2-methyl-4-heptene-6-ine and 2-methyl-4 : 5 : 6-heptatriene." The last two were studies of mixed ethylenic and acetylenic hydrocarbons, classes of compounds which formed the basis of much of Grignard's subsequent original work.

Grignard's work on organo-magnesium compounds began in 1899 and arose from Barbier's assigning to him the further study of the action of magnesium in the presence of methyl iodide on methylheptenone. Barbier himself had obtained the corresponding tertiary alcohol, dimethylheptenol, by using magnesium in place of zinc as in Saytzeff's method and had thus demonstrated that magnesium and alkyl iodides could be used to react with ketones whereas zinc cannot be employed in these conditions. In repeating Barbier's work, Grignard obtained the same inconsistent and irregular results as Barbier and it occurred to him that these might be avoided by preparing the organo-magnesium compound separately and then allowing it to react with the compound containing the functional group. He was, of course, familiar with the results obtained by Lothar Meyer and his pupils on the magnesium alkyls, which were described as infusible solids sparingly soluble in neutral solvents and spontaneously inflammable in air and carbon dioxide. He also knew that Frankland and Wanklyn had shown that the zinc alkyl halides had synthetic applications similar to those of the zinc alkyls, although they generally react more sluggishly, but Grignard anticipated that magnesium, being more electropositive than zinc, would react more easily and completely than the latter metal with alkyl halides. The great discovery that magnesium in the presence of anhydrous ether reacts with alkyl halides at the ordinary temperature, giving rise to the magnesium alkyl halides (organo-magnesians, to translate the French general and convenient expression for these compounds), many of which are very soluble in ether, followed almost at once.

The first publication of Grignard's discovery was made in a short paper communicated by Moissan to the Académie des Sciences on 11 May, 1900 (*Compt. rend.*, 1901, **132**, 336) and the immediate applications of such elegant and simple reagents were quickly developed by the author himself. Even at this time, Grignard, working without assistance, exhibited outstanding qualities of hard work and tenacity which amounted to genius and which always impressed those with whom he came into contact. In July, 1901, at the age of 30, Grignard presented his work on the organo-magnesians for the degree of Docteur ès-Sciences de Lyons, his examiners being Barbier, Gouy and Vignon. Grignard declined Moissan's invitation that he should present his thesis at Paris; he preferred to dedicate it to his own university where the discovery had been made and from which he had received so much help and inspiration. Speaking at the funeral of Grignard, Professor

Urbain said, " Les débuts de Grignard sont sans doute uniques dans l'histoire des sciences chimiques. Dès sa seconde publication, il annonce l'une des plus grande découvertes qui ait été faite dans le domaine de la chimie organique et il faut remonter aux fondateurs de cette science pour trouver l'example d'une aussi remarquable précocité d'un génie créateur cultivant les sciences expérimentales."

The importance of the discovery made by the young Grignard was quickly appreciated in France; he shared the Cahours prize of the Académie des Sciences with Fosse in 1901 and with Fosse and Marquis in 1902, in which year he also received the Berthelot medal. The wide scope of the reactions of the Grignard reagents made it impossible for any one investigator to explore all their reactions. The new reaction opened up an almost illimitable field of investigation to organic chemists generally. Some might perhaps have resented the exploitation of a discovery by so many others; Grignard, however, only regarded this in the light of collaboration and derived much satisfaction in the research activity which was based on or extended by his own original work.

In the investigations of the reactions of the organo-magnesians he had, as his first chief collaborator, Tissier, who was lecturer on chemistry and also a Senator. With him, Grignard published several papers in the *Comptes rendus* dealing with the synthesis of primary alcohols starting with trioxymethylene and the synthesis of tertiary alcohols from acid chlorides, carbonyl chloride and anhydrides. It was soon realised that the ketones are intermediate products in the latter reactions and that the ketone can only be isolated in particular cases and by checking the reaction by strong cooling.

At an early stage, Grignard investigated the action of his reagents on compounds of multiple function, in the first place the ketonic esters. In normal cases the ketonic group is the more reactive and it is thus possible to isolate tertiary alcohol-esters. If the reaction is carried to completion, Grignard showed that di-tertiary alcohols are produced, and, as shown by various other investigators, this reaction may be used for effecting asymmetric syntheses.

The constitution of the Grignard reagent has been much discussed and it would appear now that Meisenheimer's co-ordination formula $\begin{matrix}Et_2O\\Et_2O\end{matrix}\!>\!Mg\!<\!\begin{matrix}X\\R\end{matrix}$ agrees best with the observed facts, and analogous constitutions are assigned to the reagents in the presence of tertiary amines which may replace the ether normally employed. The inconclusive discussion between Grignard and Blaise was, however, useful because it led to the study of the reaction between organo-magnesians and ethylene and other glycol oxides. In this particular investigation, Grignard prepared β-phenylethyl alcohol by the following series of reactions :

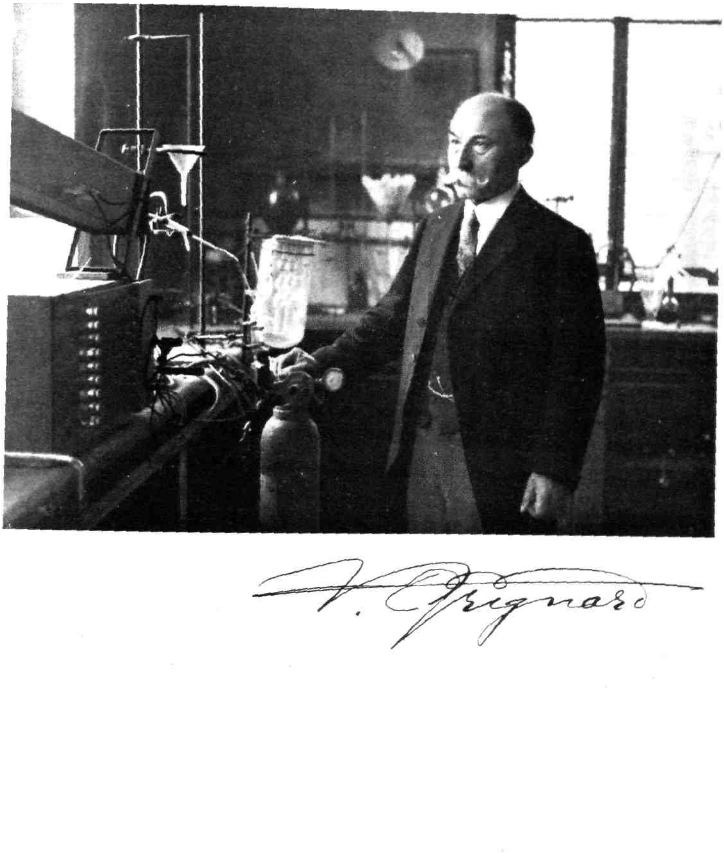
$$\begin{matrix}CH_2{\cdot}OH\\CH_2Cl\end{matrix} + MgRX \longrightarrow \begin{matrix}CH_2{\cdot}O{\cdot}MgX\\CH_2Cl\end{matrix} + RH;$$

$$\begin{matrix}CH_2{\cdot}O{\cdot}MgX\\CH_2Cl\end{matrix} + MgC_6H_5X \longrightarrow \begin{matrix}CH_2{\cdot}O{\cdot}MgX\\CH_2{\cdot}C_6H_5\end{matrix} + MgXCl \longrightarrow \begin{matrix}CH_2{\cdot}OH\\CH_2{\cdot}C_6H_5\end{matrix}$$

β-Phenylethyl alcohol is used in artificial rose perfume and this was the first industrial application of Grignard's work.

So far, Grignard's work had been carried out at Lyons, where he held a position which may be described as that of an assistant lecturer, but in November, 1905, he became lecturer at Besançon, where Boutroux, a pupil of Pasteur, was professor and was still investigating vine-must. At Besançon, Grignard carried on his investigations under restricted conditions, but began the study of the action of the reagents on thionyl chloride, thus providing a useful method for the preparation of sulphinones or sulphoxides; he returned to Lyons in the following year to collaborate again with Barbier and to direct the researches of his own co-workers.

By this time, 1906, many investigators had made considerable use of the Grignard reaction not so much for the preparation of compounds hitherto difficult of access but in the determination of constitution, and Grignard with Barbier now began to use his reagent for similar purposes. By the exhaustive hydration of French ' pinene ' (action of benzene-



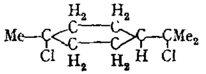
[To face p. 172.

sulphonic acid in acetic acid and hydrolysis of the resulting acetyl derivative) the α-pinene is converted into α-terpinol (m. p. 35°):

From the final residue, Grignard isolated for the first time from such a French source, camphene (m. p. 42°) and showed that *l*-limonene, dipentene (*dl*-limonene) and terpinolene were also present. Perhaps only workers in this field of organic chemistry can appreciate with what difficulties such work at that time was attended.

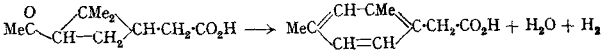
Grignard next investigated the solid and liquid pinene hydrochlorides which had been described by Barbier in 1883. He showed that each of these hydrochlorides reacts with magnesium and by oxidation and subsequent decomposition of the magnesium derivative of the liquid hydrochloride obtained a mixture of alcohols having the formula $C_{10}H_{18}O$, among which the chief are borneol and fenchyl alcohol. By the action of carbon dioxide on the same magnesium derivative, Grignard isolated an acid, $C_{11}H_{18}O_2$, together with a complex terpene and a hydrocarbon, $C_{20}H_{34}$, indicating the joining together of the original radicals under the action of magnesium. By the oxidation of the magnesium derivative of the solid hydrochloride, Grignard obtained a mixture of borneol and *iso*borneol and by the treatment of the same magnesium derivative with carbon dioxide he isolated what we now know to be *cis*- and *trans*-camphane-2-carboxylic acids.

In investigating the action of magnesium on dipentene dihydrochloride (of which two, *cis*- and *trans*-, forms are known), Grignard showed that this compound behaves similarly to αε-dibromopentane, in giving a dimagnesium derivative. Under the influence of the



metal two molecules of hydrogen chloride may be lost with the regeneration of dipentene; further, two monomagnesium derivatives may be formed, proving the removal of a molecule of hydrogen chloride in two different directions. The action of carbon dioxide on the magnesium derivative of the crude dihydrochloride gives rise to two monocarboxylic acids and the two stereoisomeric dicarboxylic acids indicated by theory. The dehydration of the *cis*-dicarboxylic acid led to the synthesis of a ketone, $C_{11}H_{16}O$, indicating a loss of two hydrogen atoms, whereas the formation of a ketone, $C_{11}H_{18}O$, might ordinarily be expected.

In collaboration with Barbier, Grignard prepared the *l*- and *d*-pinonic acids in a state of purity and described their properties in detail. The former prepared by the oxidation of *l*-pinene differed from that obtained by Tiemann by oxidising sodium *l*-α-campholenic acid and distilling the *l*-α-dihydroxydihydrocampholenic acid. By the action of bromine in the presence of water at 200°, Grignard was able to convert pinonic acid into *m*-xylene-4-acetic acid, the following reaction taking place:



This is an interesting example of the conversion of a terpene into an aromatic derivative.

Grignard had an extremely systematic mind and his work in terpene chemistry led him to consider in detail the current nomenclature of organic compounds. His first publication on this subject was in 1910 and his appointment in 1912 as a member of the Commission of Organic Nomenclature was specially appropriate. Although he did not become a member of the Commission of the Union Internationale de Chimie after the War, his

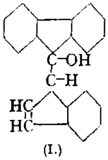
criticisms, published in 1927 and 1928, of the preliminary findings of the Commission were extremely logical and useful to the Commission.

At about this time, Grignard devised his method for the more effective inter-condensation of aldehydes, by dissolving the aldehyde in a sufficient quantity of an appropriate solvent (generally ether) and allowing this to react at a suitable temperature with rapid stirring with an energetic condensing agent (alkali sulphite or alkali hydroxide) dissolved in a small quantity of water or other solvent only slightly miscible with the former. The successive 'aldolisation' of small quantities of the aldehyde in the aqueous solution *of the condensing agent and successive removal of the aldol from the aqueous solution* by the ether not only gave increased yields of the aldols but reduced the formation of polymerised derivatives to a minimum.

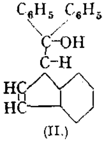
The numerous simple and mixed aldols so prepared were converted into the corresponding unsaturated aldehydes, which were then treated with organo-magnesians; similarly from these aldols, unsaturated and saturated alcohols were prepared and characterised. From the latter, Grignard prepared and studied in detail a number of new *ethylenic hydrocarbons: from the former, he obtained a considerable number of complex* hydrocarbons having two double bonds, whose derivatives were also investigated. The alcohols and their derivatives were similarly investigated, and the physical constants of all these related substances carefully determined. The determination of the molecular refractions of this series of compounds formed an important addition to our knowledge of the relationship between constitution and molecular refraction.

In 1909 Grignard was appointed to take charge of the department of organic chemistry at Nancy in succession to Blaise, who had been appointed to Paris on the death of Bouveault. In the following year, at the age of 40, Grignard became Professor of Organic Chemistry at Nancy, succeeding to a well-equipped department having a great reputation established by Haller and maintained by Bouveault and Blaise.

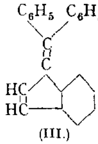
One of Grignard's most important investigations at Nancy, with Courtot as collaborator, had indene as its starting point. In view of the fact that indene forms a sodium derivative, Grignard concluded that it should also form a magnesium derivative and he prepared the sparingly soluble magnesium indenyl bromide, $C_6H_4<\begin{matrix}CH\\CHMgBr\end{matrix}>CH$, by the action of organo-magnesium bromides on indene. By the usual methods, 1-indenol and indene-1-carboxylic acid were also isolated. By the action of magnesium indenyl bromide on fluorenone at 120° Grignard obtained *tert.*-1-indenylfluorenol (I). By a similar reaction



(I.)

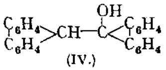


(II.)

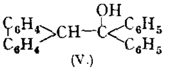


(III.)

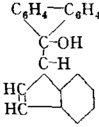
with benzophenone, he isolated 1-indenyldiphenylcarbinol (II), part of which suffered loss of water, producing the orange-coloured diphenylbenzfulvene (III). He extended this



(IV.)



(V.)



(VI.)

work to *cyclo*pentadiene and to fluorene, the magnesium derivative of the latter being prepared at 135° in xylene, and obtained derivatives of these hydrocarbons analogous to

those of indene. He isolated, for example, *tert.*-fluorenylfluorenol (IV) and certain derivatives as well as fluorenyldiphenylcarbinol (V) and *tert.*-1-indenylfluorenol (VI). The preparation of the benzfulvenes and dibenzfulvenes by the dehydration of the above compounds as well as from the magnesium derivative of *cyclo*pentadiene followed naturally and made these compounds comparatively easy of access.

At the same time, Grignard and his pupils were occupied with the synthesis of cyanides by the action of organo-magnesians on gaseous cyanogen chloride and on cyanogen. In the former case, Grignard described the actions as follows:

$$RMgX + Cl{\cdot}C{\vdots}N \longrightarrow Cl{\cdot}CR{:}NMgX \longrightarrow RCN + MgXCl$$

and in the latter case as

$$RMgX + (CN)_2 \longrightarrow N{\vdots}C{\cdot}CR{:}NMgX \longrightarrow RCN + NCMgX$$

Grignard showed that cyanogen halides are capable of reacting not only as indicated above but also, particularly cyanogen bromide and iodide, thus:

$$XCN + MgRX' \longrightarrow RX + MgCNX' \quad (X \text{ and } X' = Br, I)$$

With cyanogen iodide this is the chief reaction; with cyanogen bromide, both reactions occur, although the latter predominates. This reaction for introducing bromine and iodine has proved useful in several instances for the preparation of halogen derivatives not otherwise easily accessible, as, for example, in the preparation of halogen derivatives of acetylenic hydrocarbons:

$$R{\cdot}C{\vdots}C{\cdot}MgBr + BrCN \longrightarrow R{\cdot}C{\vdots}CBr + MgBrCN$$

An important extension of this investigation was the method of preparing ketones by acting with two molecular proportions of magnesium alkyl or aryl halide on one molecular proportion of cyanogen chloride, the reactions taking place being:

$$Cl{\cdot}C{\vdots}N + MgRX \longrightarrow Cl{-}\underset{R}{\overset{|}{C}}{:}N{\cdot}MgX$$

$$Cl{\cdot}CR{:}NMgX \xrightarrow{MgRX} {}^{R}_{R}{>}C{:}NMgX + MgXCl$$

$${}^{R}_{R}{>}C{:}NMgX + H_2O \longrightarrow {}^{R}_{R}{>}C{:}NH + MgX{\cdot}OH$$

$${}^{R}_{R}{>}C{:}NH + H_2O \xrightarrow{acid} {}^{R}_{R}{>}CO + NH_3$$

The Nobel Prize for Chemistry in 1912 was divided between Professor Paul Sabatier (also an Honorary Fellow of our Society) for his method of catalytic hydrogenation and Professor Victor Grignard for his discovery of the organo-magnesium compounds. Grignard received the award with becoming modesty and when he was being acclaimed by his colleagues and students at Nancy he said "La récompense suédoise aurait dû d'abord être décernée à Sabatier et Senderens, puis plus tard c'eût été mon tour de la partager avec Barbier." On this and many other occasions, Grignard was always ready to acknowledge his indebtedness to his 'maître vénéré,' and Barbier, pleased with the independent recognition of his pupil, said, "Grignard a rappelé la parte légitime qui lui revient dans une telle découverte. Mais le réactif préparé simplement comme nous venons de le décrire est de Grignard seul et c'est la découverte de ce réactif aux aptitudes réactionnelles infinies, que récompensait l'aréopage de Stockholm."

After the annual meeting in July, 1914, of the French Association for the Advancement of Science at Le Havre, in which Grignard had taken a prominent part, he went to Saint-Waast-la-Houge for his annual holiday; and it was there that Grignard was mobilised in his former rank of corporal, the rank which he had attained during his military service in 1893, becoming a coast-guard at Cherbourg before he was called to carry out chemical investigations of national importance. Grignard spent nearly a year investigating new or unexplored sources of toluene at Nancy and was then transferred to Paris to work in connexion with gas warfare in Urbain's laboratory at the Sorbonne. He investigated the

preparation of phosgene by the action of oleum on carbon tetrachloride. The chlorosulphonic acid, a by-product in the reaction

$$H_2SO_4 + SO_3 + CCl_4 \longrightarrow COCl_2 + HClSO_3,$$

was converted into the ethyl ester by treatment with ethylene, and this ester proved to have lachrymatory properties. Grignard showed that the following reaction can be brought about at about 80° in the presence of certain catalysts and particularly by infusorial earth,

$$2H_2SO_4 + 3CCl_4 \longrightarrow 3COCl_2 + 4HCl + S_2O_5Cl_2$$

This rendered the use of oleum or sulphuric anhydride unnecessary for this method of producing phosgene. The pyrosulphuryl chloride was isolated as a chemical individual and, later, from its physical constants Grignard suggested that its constitution is O:S(OCl)·O·(OCl)S:O.

Like many other workers at this time, Grignard studied the conditions for the chlorination of methyl formate and methyl chloroformate; he established the conditions for the production of mono-, di-, and tri-chloromethyl chloroformates and determined their physical constants.

Cyanogen bromide and iodide are useful lachrymators produced readily by the action

$$X_2 + MCN \longrightarrow XCN + MX \quad (X = Br \text{ or } I,\ M = Na \text{ or } K)$$

but one half the bromine or iodine is 'lost' for the immediate purpose. Grignard showed that, whereas chlorine liberates bromine and iodine from alkali salts, it does not react appreciably with cyanogen bromide and iodide at the ordinary temperature; by passing chlorine into the reaction mixture, the bromine or iodine liberated can then react with a fresh quantity of the alkali cyanide.

Grignard's test for 'yperite' or mustard gas still remains the most convenient for field work. It consists in converting the compound into the more readily crystalline ββ′-di-iododiethyl sulphide by the reaction

$$2NaI + (CH_2Cl{\cdot}CH_2)_2S \longrightarrow 2NaCl + (CH_2I{\cdot}CH_2)_2S$$

Using a simple apparatus, Grignard showed that it is possible to detect 0·01 gram of mustard gas in 1 cubic metre of air.

The French Academy of Sciences encouraged its members to continue the publication of their previous investigations in so far as their military duties permitted and at this time (1916) Grignard published an account of a method of obtaining mercurated aromatic alcohols, a class of compounds previously unknown. He showed, for example, that when ω-chloromercuriacetophenone reacts with ethyl magnesium bromide, the ketonic group is attacked, resulting in the production of α-chloromercuri-β-phenylbutan-β-ol, $CEtPh(OH){\cdot}CH_2{\cdot}HgCl$. Similarly, *o*-chloromercuribenzophenone gives α-phenyl-*o*-chloromercuriphenylpropan-α-ol, $CEtPh(OH){\cdot}C_6H_4{\cdot}HgCl$.

From August, 1917, until January, 1918, Grignard, now promoted to 2nd Lieutenant, was in America as representing Chemistry in M. Tardieu's "Mission d' Etudes." After demobilisation (February, 1919), Grignard returned to his professorship at Nancy, but in November of the same year he was appointed professor at Lyons in succession to Barbier, who had just retired under the age limit.

In continuation of his work on the dehydration of alcohols, Grignard investigated the cases of those obtained by the action of organo-magnesians on methylheptenone, which exists in two isomeric forms:

$$CH_3{\cdot}\underset{\underset{CH_2}{\|}}{C}{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}CH_3 \ (\alpha) \qquad \begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}CH_3 \ (\beta)$$

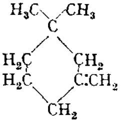
The aliphatic alcohols obtained from the β-form when submitted to dehydration with metaphosphoric acid yield dienes chiefly of the form (VII). The dienes derived from the

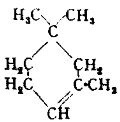
$$(VII.)\ \begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}C\!\!<\!\!\begin{matrix}CH_3\\R'\end{matrix} \qquad \begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}C\!\!<\!\!\begin{matrix}CH_2\\R\end{matrix}\ (VIII.)$$

(R′ = methylene or substituted methylene)

aromatic alcohols (R = Ph or Bz) on the other hand have the constitution (VIII). When anhydrous oxalic acid is used as the dehydrating agent, the lower members of the aliphatic

series yield γ- and α-*cyclo*geraniolenes, (I) and (II) respectively, the latter being present in variable proportions and in less quantity.

(I.) 

 (II.)

Many years previously, Grignard had observed that, when *iso*amyl magnesium bromide reacts on acetone, small quantities of mesityl oxide and phorone are produced, and similar observations are recorded by other investigators. Subsequently, Grignard showed that condensation of aldehydes and ketones between themselves took place during the Grignard reaction, yielding unsaturated ketones. He correlated this type of condensation with what he described as the Cannizzaro–Tistchenko condensation, described for the first time by Franke and Kuhn in the case of α-methyl-α-hydroxymethylpropaldehyde (formyl-*iso*butyl alcohol)

$$2HO{\cdot}CH_2{\cdot}CMe_2{\cdot}CHO \longrightarrow \underset{\text{hydroxypivalyl hydroxypivalate}}{HO{\cdot}CH_2{\cdot}CMe_2{\cdot}CO{\cdot}O{\cdot}CH_2{\cdot}CMe_2{\cdot}CH_2{\cdot}OH}$$

Grignard suggested that such condensations occurring under the influence of aluminium and magnesium alcoholates might be induced by magnesium halogen alcoholates, Mg(OR)X, which are normal products of the Grignard reaction. He showed that in ethereal solution these mixed alcoholates exhibit towards aldehydes and ketones much greater condensing powers than the ordinary alcoholates. They are capable, for example, of condensing ketones of which both radicals contain more than one carbon atom, such as diethyl ketone and dipropyl ketone; the condensing power increases from chlorine to iodine and is greater when tertiary radicals are present than for primary and secondary. Grignard's suggested mechanism of the condensation is: (1) addition of the alcoholate to the aldehyde or ketone, and (2) reaction of this complex with another molecule of the aldehyde or ketone:

$$R{\cdot}CH_2{\cdot}CH{<}^{OMgX}_{Oalk.} + H{\cdot}\overset{R}{C}H{\cdot}CHO \longrightarrow R{\cdot}CH_2{\cdot}CH{<}^{OMgX}_{CHR{\cdot}CHO} + alk.OH$$

He suggested that ester production took place *via* the ' hemiacetal,'

$$R{\cdot}CH_2{\cdot}CH{<}^{OMgX}_{Oalk.} + {}^{alk.O}_{XMg{\cdot}O}{>}CH{\cdot}CH_2R \longrightarrow R{\cdot}CH_2{\cdot}CH{<}^{O}_{O}{>}CH{\cdot}CH_2R + 2\ alk.O{\cdot}MgX$$

$$\downarrow$$

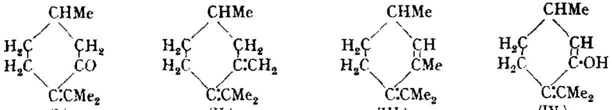
$$R{\cdot}CH_2{\cdot}CO{\cdot}O{\cdot}CH_2{\cdot}CH_2R$$

The reducing action of organo-magnesians has been observed by many workers, and Grignard's explanation of the formation of benzyl alcohol together with *iso*amylphenylcarbinol by the action of *iso*amyl magnesium bromide on benzaldehyde in breaking down the hemiacetal is:

$$C_6H_5{\cdot}CH{<}^{OMgBr}_{O{\cdot}CH_2{\cdot}C_4H_9} \longrightarrow C_6H_5{\cdot}CH_2{\cdot}O{\cdot}MgBr + C_4H_9{\cdot}CHO$$

Two of Grignard's important contributions to terpene chemistry were in connexion with pulegone and citronellol. By the action of methyl magnesium iodide on pulegone (I) he obtained a hydrocarbon to which he assigned constitution (II). Subsequent work has shown that this hydrocarbon is not homogeneous but probably a mixture of (II) and (III). In further work, Grignard showed that the volume of gaseous hydrocarbon evolved increased with increasing weight of the alkyl group (in the alkyl magnesium halide) and with that of the halogen; he showed further that the oil recovered from the reaction is not pulegone but its enolic form, pulegenol (IV), which he characterised as its benzoyl derivative. The

fixation of the enolic form is due to the formation of a magnesium organo-enolate, a corresponding volume of gaseous hydrocarbon being liberated.



(I.) (II.) (III.) (IV.)

Grignard and his pupils made a notable contribution to chemistry in resolving the citronellol–rhodinol question. *d*-Citronellol was prepared in three ways: (i) from Java citronella oil, (ii) by the reduction of *d*-citronellal, and (iii) by the reduction of the acetyl derivative of the enolic form of *d*-citronellal. The material from each source was submitted to the action of ozone. Each specimen was found to be a mixture of the two alcohols (V) and (VI). The percentage composition of the mixtures determined from the amounts

(V.) (VI.)

of acetone and formaldehyde formed was between 76 and 81% of (V) and between 24 and 18% of (VI). *dl*-Citronellol synthesised from methylheptenyl bromide gave similar results on ozonolysis. They then prepared rhodinol by standard methods and showed that it had similar physical properties and the same chemical properties as citronellol and gave the same results on ozonolysis. Grignard's investigations in this field were carried out with the utmost care and left no doubt that citronellol and rhodinol are identical, both being mixtures of the two alcohols (V) and (VI).

The versatility of Grignard as a chemist is well illustrated by his investigations of catalytic dehydration and reduction at pressures lower than that of the atmosphere and at various temperatures, which resulted in different products according to the pressure and temperature at which the particular process was carried out. Thus, he obtained a yield of 67% of benzyl alcohol by reducing benzaldehyde at 150° and 100 mm., the unchanged aldehyde being recovered. By lowering the temperatures and pressure and using nickel as a catalyst, he was able to increase the proportion of the enolic form of benzylideneacetone, showing that 1 : 4 addition proceeds simultaneously with that normally taking place at the ketonic double bond. In the case of the reduction of phenol in *cyclo*hexanol solution, Grignard was able to isolate tetrahydrophenol, $CH_2{<}{CH_2{\cdot}CH_2 \atop CH_2{-}CH}{>}C{\cdot}OH$, which apparently constitutes the first phase of the hydrogenation; the enolic form of *cyclo*hexanone later may become ketonic or be further reduced to the cyclic secondary alcohol. Grignard also obtained the enolic forms of 4-methyl*cyclo*hexanone and carvomenthone. Using platinum oxide as a catalyst at about 200° and at pressures varying from 140 to 400 mm., he showed that benzoyl chloride, phenylacetyl chloride and phenylpropionyl chloride were hydrogenated to the corresponding aldehydes without any appreciable formation of the by-products always produced at ordinary pressure. Unfortunately by this method only poor yields of the corresponding aldehydes are obtained from aliphatic acid chlorides.

Unsaturated hydrocarbons of various types and their derivatives provided a fruitful field of investigation for Grignard and his pupils for many years. From acetylenic magnesium halides of the type R·C⋮C·MgX, Grignard prepared a series of conjugated diacetylenes by the action of two atomic proportions of iodine on two molecular proportions of the reagent. He thereby obtained $\Delta^{\delta\epsilon}$-decadi-inene, $\Delta^{\epsilon\eta}$-dodecadi-inene, $\Delta^{\xi\theta}$-tetradecadi-inene, and αδ-diphenyldiacetylene. The last compound when submitted to catalytic hydrogenation gave three compounds, thus,

CPh⋮C·C⋮CPh → CHPh:C:C:CHPh (αδ-addition)
CPh⋮C·C⋮CPh → CHPh:CH·CH:CHPh (αβγδ-addition)
CPh⋮C·C⋮CPh → $CH_2Ph{\cdot}C{\vdots}C{\cdot}CH_2Ph$ (ααδδ-addition)

Since the days of Sir Edward Frankland, the preparation and investigation of organo-metallic compounds have been carried out by many workers chiefly for the purpose of solving problems in valency and stereochemistry. These compounds were first prepared by the action of the zinc alkyls and later by means of the organo-magnesians. It is somewhat interesting that this type of investigation did not greatly appeal to Grignard himself; his only excursion into this field resulted in the preparation of aluminium diethyl iodide and aluminium ethyl di-iodide. He found that these compounds are of little use under such conditions as the Friedel–Crafts reaction and they do not react with carbon dioxide or, in general, like the organo-magnesians.

Grignard had for long contemplated the production of a comprehensive treatise in French on Organic Chemistry, a project which Moureu had previously had in view, and at length announced the publication of a "Traité de Chimie organique" in fifteen small quarto volumes. The first volume appeared in 1935 and four volumes, all edited by Grignard, have already been published. There is reason to believe that the labour involved in this work was too great a tax on the strength of one already overworked.

Many honours came to Grignard and were accepted with a quiet dignity which was characteristic. He was a Commander of the Légion d'Honneur and became member of the Académie des Sciences in 1926. He was an honorary member of the Chemical Societies of England, France, America, Belgium, Roumania and Poland, and of the French Society of Chemical Industry, an honorary member of the Royal Society of Sciences of Upsala, and Roumania, a corresponding member of the Polish and Roumanian Academies, and held the Doctorate, *honoris causa*, of the Universities of Brussels and Louvain.

With the exception of one year at Besançon and about four years as Professor at Nancy, the whole of Grignard's academic life was spent in the University of Lyons. The spirit of centralisation is strong in France and is well expressed by Pasteur's pronouncement on a promising young man—"Ce jeune homme se placera rapidement au nombre de nos mathématiciens les plus éminents. Il faut absolument qu'il reste à Paris." In spite of the lustre attaching to an office in the capital Grignard refused at least two requests to accept a professorial chair in Paris. Although a man of great personal charm and force of character, he feared that absorption by administrative duties which always await competent scientific workers in the metropolis. With that modesty which was recognised by all who knew him, Grignard preferred the academic quiet of Lyons, and the opportunity it provided for the undisturbed continuance of his research work. He died on December 13th, 1935, and was buried at Lyons. His pupil, collaborator and friend, Professor Ch. Courtot, has recently published a comprehensive account of his work in the *Bulletin de la Société chimique de France.**

C. S. GIBSON.
W. J. POPE.

JAMES FRANCIS HALPIN.

1866—1936.

JAMES F. HALPIN was born at Limerick on August 3rd, 1866. He was educated at Camelford School, Cornwall, and studied chemistry at King's College and the Royal College of Science, London.

After some experience with the Excise Department Halpin was appointed in 1892 to the Government Laboratory, then occupying a part of Somerset House. In this department Halpin spent the major part of his official career, and retired with the rank of Superintending Chemist in 1929.

His work in the Government Laboratory was concerned chiefly with the chemical control of the Customs and Excise duties on beer, sugar, wine and spirits, and investigations in connexion therewith. In the course of his work he acquired an exceptional knowledge of

* In the photograph accompanying this notice, Grignard is standing in his laboratory at Lyons before his apparatus for carrying out hydrogenations under reduced pressures at the same place where he first prepared the Grignard reagent.

Revenue questions, and his special experience was utilised on a number of Departmental committees to which he was appointed.

In addition to the chemical side, Halpin possessed an intimate knowledge of the historical, legal, and administrative aspects associated with Customs and Excise duties and he never wearied of imparting valuable information and advice on questions pertaining to the Revenue to his staff and colleagues.

When he retired from the Government Chemist's Department he was awarded the Imperial Service Order.

Halpin was always energetic and it was not surprising, therefore, that within a year of his retiral from the Government Laboratory he re-entered active employment when he became Director of the Egyptian Government's Tobacco Laboratory at Cairo. He served in that capacity for four years, finally returning to England in 1934. He died after a short illness on June 21st, 1936.

In his spare time Halpin was an omnivorous reader. He enjoyed long tramps in the countryside and was an enthusiastic observer of bird life. He had a quiet unassuming manner and an even-tempered and courteous disposition. His relations with his staff and colleagues were ideal and he was greatly missed when he left the Government Laboratory.

Halpin was a Fellow of the Chemical Society and of the Institute of Chemistry. He is survived by his widow, one son, and a daughter.

A. J. H. GAUGE.

HENRY REGINALD HIRST.

1876—1936.

HENRY REGINALD HIRST was born at Batley in 1876, the eldest son of the late Mr. G. H. Hirst, owner of the well-known woollen mills which still run under the title G. H. Hirst & Co., Ltd.

Hirst received his early education at the Wheelwright Grammar School, Dewsbury, and proceeded to the University of Leeds, where he graduated B.Sc., Honours in Chemistry, in 1905; he received the degree of M.Sc. in 1929. He was a Fellow of the Chemical Society, a Fellow of the Institute of Chemistry, a member of the Institute of Chemical Engineers, a member of the Society of Dyers and Colourists, and a member of Committee of the Bradford Textile Society.

On leaving the University Hirst entered the family business and here laid the foundations of his wide knowledge of technical processes in the woollen industry. Despite the fact that during the war his firm were busily employed on army clothing contracts, he was anxious to take a more active part and joined the forces in 1915. After a period of general training he was transferred to the ordnance inspection depot near Rouen, where he was responsible for the examination of all types of ammunition passing through the centre. He received official recognition for " Coolness and gallant conduct at an ammunition base on July 3rd, 1917, in helping to put out a fire on board an ammunition ship."

In 1920 Hirst joined the newly formed British Research Association for the Woollen and Worsted Industries, now the Wool Industries Research Association, and at the time of his death was its chief Technologist. Although apparently in excellent health, he had a sudden heart attack and died at his home on December 10th, 1936.

Hirst evinced an especial interest in finishing processes, and for research on such processes his experience gained in industry was most valuable. His interest in milling processes caused him to carry out fundamental work on the swelling of wool fibres when placed in various solutions, and more technical researches dealt with methods for increasing the rate of milling by suitable pre-treatment of the cloth, thus effecting a saving in time and enabling production to be increased. Much of his work concerned the elucidation of the causes of defects in materials, and in this work his interest did not cease with the resolution of a particular problem, but he was at all times keenly alive to the desirability of devising methods for the prevention of such defects. He was a pioneer in the study of the causes and prevention of mildew and worked out satisfactory methods for its prevention and made

clear the conditions under which wool is liable to mildew attack. Perhaps his greatest interest was in dyeing processes and related problems. In 1925 he suggested a general scheme of test to be applied in the determination of fastness of dyes to wool to various agencies, *e.g.*, light, washing, perspiration, stoving, etc. He was a member of the Committee of the Society of Dyers and Colourists which in later years initiated and carried out comprehensive investigations on standard methods of test for fastness to light, washing, and perspiration for all types of coloured textile materials.

The demands of his work led Hirst to develop new analytical methods and he was ever ready to take advantage of advances in other branches of science and apply them to his own particular problems. An outstanding example of this is the great use he made of ultra-violet radiation as an aid in textile analysis, especially in the examination of oil stains. He was greatly interested in photography both as a hobby and as an aid in his work, and at the time of his death was developing the methods of fluorescence photography for the examination of defects caused by oil stains.

Although keenly alive to the general problems of the day, Hirst evinced little interest in politics until recent years, when he became a keen supporter of the Social Credit Party. Many of his spare evenings were spent in attending and giving lectures on this subject. His leisure was spent in the country, where he had a small estate and took much delight in the growing of choice fruits.

His death, though tragic in its suddenness, may also be regarded from the point of view of a classical authority who said many centuries ago " It is a sign of a fortunate man to die before he calls on death."

W. I. R. A.

JAMES HENRY HOSEASON.

1869—1936.

JAMES HENRY HOSEASON, who died on September 22nd, 1936, at his home, St. Michael's Mount, Hankham, Sussex, aged sixty-seven years, was born at Chefoo, China, on February 18th, 1869. His father, a native of the Shetland Islands, was a captain in the Mercantile Marine and incidentally was able to teach his son Greek. Hoseason was educated in Edinburgh, served an apprenticeship to pharmacy in that city, and had further experience under John B. Stephenson, Chairman of the Board of Examiners (Scotland) of the Pharmaceutical Society. He received his scientific training at the Heriot-Watt College, Edinburgh, during the professorships there of W. H. Perkin, jnr., and F. Stanley Kipping. Having obtained the qualification of pharmaceutical chemist, he was appointed, in 1891, Assistant Lecturer in Materia Medica, Pharmacy and Pharmaceutical Chemistry, under Professor D. J. Leech, M.D., at Owens College, Victoria University, Manchester, with entire charge of the Pharmaceutical Department. Resigning this appointment in 1896, he entered upon a commercial career and in 1900 became partner and works manager in the firm of Hough, Hoseason & Co., manufacturing chemists, Manchester, and remained there until his retirement some twelve years ago. He did a large amount of research work on digitalis and on the production of artificial shellac. This he made in limited quantities, founding the Anglo-Indian Manufacturing Co., but the venture was abandoned after five years' existence. He also published various papers and notes on pharmaceutical subjects from the year 1889 on. He was elected a Fellow of the Chemical Society on February 18th, 1909, and his interest in scientific matters remained unabated after his retirement.

JAMES GRIER.

EMANUELE PATERNÒ.

1847—1935.

EMANUELE PATERNÒ DI SESSA, the bearer of an old Sicilian family name, was born in Palermo on December 12th, 1847, shortly before his father, who was implicated in the revolution of 1848, was exiled and left, with his wife and family, for Egypt. After the

death of the father at Alexandria in 1858, the mother settled in Genoa with her sons, not caring to return to Sicily under the domination of the Bourbons. The family returned to Palermo in 1860 and in due course young Paternò commenced his higher education under Naquet, then Professor of Chemistry at the Technical College. He worked later under Cannizzaro at the University of Palermo and took his Doctorate in Physics and Chemistry in 1871.

Lieben, who was Assistant Director of Cannizzaro's Laboratory at Palermo from 1863 to 1867, had done much to explain the production of chloral from alcohol and chlorine and Paternò's first original work was devoted to the detailed study of the reactions concerned. He thus isolated trichloroacetal, prepared dichloroacetaldehyde from the corresponding acetal, and obtained pure pentachloroethane by treating chloral with phosphorus pentachloride in 1869; a little later he obtained tetrachloroethylidene dibromide by the action of bromine on pentachloroethane and prepared several other highly chlorinated and brominated methanes and ethanes. He did not confine himself to problems related to chloral but at the same time studied the formation of phenylpropiolic acid from phenylacetylene and worked with Koerner on the sulphonation of iodobenzene and with Amato on the synthesis of crotonaldehyde from acetaldehyde and ethylidene chloride.

In 1875 Paternò noted that 3-nitrocuminic acid was converted into a red amorphous product by sunlight and he continued the study of the chemical action of light for many years. Thus he demonstrated the formation of propyl butyrate by the action of light on butyric acid and carried out a number of other interesting photo-syntheses, some of which may be reproductions of actual plant syntheses. Among the condensations thus effected may be mentioned the production of αββ-triphenylhydracrylic acid,

$$(C_6H_5)_2C(OH)\cdot CH(C_6H_5)\cdot CO_2H,$$

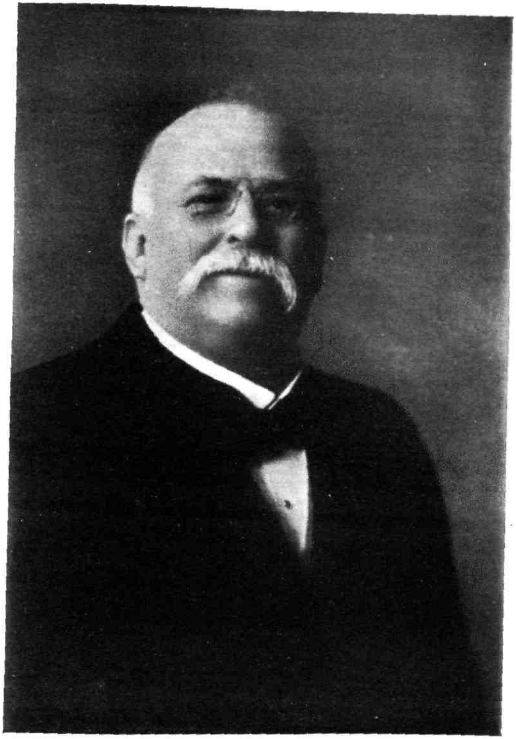
by the action of sunlight on benzophenone and phenylacetic acid in benzene solution.

At the time when Paternò was interesting himself in the halogen derivatives of the simple paraffins two modifications of ethylene dichloride were supposed to exist; to explain this he introduced in 1869 the conception of the tetrahedral configuration of methane and published diagrams indicating the conceivability of a kind of *cis*- and *trans*-isomerism of ethylene dichloride, without postulating, of course, free rotation of the carbon atoms. Some controversy has arisen in later days on the question as to whether Paternò should receive priority over van 't Hoff and Le Bel in connection with the conception of the asymmetric carbon atom. The idea that a quadrivalent atom is tetrahedrally environed dates at least from Wollaston in 1808 and Paternò claimed no credit in this connection; the notion of asymmetry as applied to the optical activity of methane derivatives dates from the publications of van 't Hoff and Le Bel in 1874. It is interesting, however, to note that Debye was endeavouring in 1930 to obtain evidence by *X*-ray analysis of the existence in gaseous ethylene dichloride of two isomerides corresponding in configuration to the isomerides foreshadowed by Paternò more than sixty years before.

In 1870 Paternò published a short paper in the *Gazzetta* showing that carbonyl chloride is formed readily by the catalytic action of animal charcoal on a mixture of carbon monoxide and chlorine. This reaction is interesting, first because it is probably the earliest example of the use of carbon as a catalyst, and, secondly because most samples of animal charcoal have no catalytic action on the mixed gases. For long after Paternò's publication phosgene was manufactured for technical purposes by exposing carbon monoxide with chlorine to sunlight in glass carboys; it was ultimately found, however, that properly prepared charcoal catalyses the reaction with great rapidity and Paternò's method is now used exclusively for the technical manufacture of phosgene.

Paternò was greatly interested in natural products; he carried out an extensive investigation of cymene from various sources, and studied such components of lichens as usnic acid. His work on lapachic acid or lapachol, published in 1882, is monumental and established that this substance is a derivative of α-naphthaquinone. He interested himself in organic fluorine compounds and, in collaboration with Olivieri, was the first to prepare fluorobenzene; these co-workers characterised the three fluorobenzoic acids in 1882.

Paternò was one of the first to be attracted by the work of Raoult on the depression



Emanuele Paternò

[To face p. 182.

of the freezing point of solvents by solutes and its bearing on the determination of molecular weights. In conjunction with Nasini he showed that citraconic, itaconic and mesaconic acids have the same molecular formula and hence are not related as polymerides. They showed that bromine has the composition Br_2 in aqueous solution and that in benzene sulphur has the molecular composition S_8. He did a good deal of work on colloidal solutions and was the first to advance the view, in 1889, that such substances as gallic and tannic acids exist in aqueous media as suspensions of swollen particles which are still sufficiently small to pass through filter paper.

In 1871, when only twenty-four years of age, Paternò started the *Gazzetta di Chimica Italiana* and, fifty years later, when handing the journal over to the Associazione Italiana di Chimica Generale ed Applicata, he reprinted in the *Gazzetta* all his early papers which had appeared in the *Giornale di Scienze Naturali ed Economiche di Palermo*, so that, as he said, all his contributions to Chemistry should appear in the same journal. In the preface to volume 50 of the *Gazzetta*, in relinquishing the Editorship, he recounted the early financial difficulties of the publication and tells how Cannizzaro, who was joint Editor with himself, foreboding failure, insisted on the journal appearing anonymously. In an earlier issue, that of January, 1883, Paternò gave a description of the teaching and research work done in the Chemical Laboratory of the University of Palermo during his tenure of office—from 1872—and describes how an unsuitable building had been made to serve and a poor financial subvention had been applied, as he said—" e Dio sa come," yielding results of which he was justifiably proud. He noted that the laboratory subvention amounted to about £300 per annum but its old students, Fileti, Ogilaloro, Spica and Mazzara, trained under him, had all been appointed to professorial chairs. In 1923 the Associazione Italiana di Chimica established a gold medal in honour of Paternò to be awarded trienially for the most important piece of chemical work done during the preceding ten years; the first recipient of the medal was F. W. Aston of Cambridge.

Paternò became Professor of Chemistry in the University of Palermo when Cannizzaro was appointed to the Chair at Rome in 1872. He went to Rome as Professor of Applied Chemistry in 1893 and, on Cannizzaro's death in 1910, was elected Professor of General Chemistry and Director of the Chemical Institute in the University; he retired from teaching work in 1923 at the age of 75 as Emeritus Professor. Throughout his active life Paternò filled many municipal and government offices; he had been Rector of the University of Palermo and became a Senator of the Kingdom in 1890, serving for many years as Vice-President of the Italian Senate. He received the honorary Sc.D. of the University of Cambridge in 1912 and was elected an honorary Fellow of the Chemical Society in 1920; he became a National member of the Accademia dei Lincei in 1883 and a Foreign Associate of the Académie des Sciences in 1923. He died in Palermo on January 18th, 1935.

Paternò was a thick-set sturdy figure full of energy and vivacity. Although his interests in chemical science and technology were wide, as is shown by his publications, he had a vast knowledge of world affairs, stimulated no doubt by the political turbulence amid which his early days were spent. He was a charming personality, a lively and humorous conversationalist, and a delightful companion even to those much younger than himself.

W. J. Pope.

WILLIAM RINTOUL.*

1870—1936.

William Rintoul died at the age of sixty-six years at his home in Ardrossan, Ayrshire, on August 25, after nearly a year's illness. His career had been a remarkable one, and began in Glasgow, where he was educated and received in Glasgow and West of Scotland Technical College his scientific training. In the late 'eighties there were (as there are even now) few schools of analytical chemistry, so that Mr. R. R. Tatlock not only filled the post of city analyst but also himself lectured and had a staff of lecturers on chemistry and

* Reprinted by permission from *Nature*.

physics to students many of whom afterwards became his assistants and later occupied important positions in the chemical profession. Ramsay was one of them.

After a short time as an assistant, Rintoul lectured to Tatlock's students until in 1891 a post of chemist offered in a paint manufacturer's near London, where he got chemical and works experience. After three years there he went in 1894 to the Royal Gunpowder Factory as a chemist in the laboratory, later becoming chemist-in-charge of the manufacture of nitroglycerine, and for two years before he resigned he was chief chemist in the laboratory.

At this time the Royal Gunpowder Factory under Sir Frederic Nathan as superintendent and Mr. James Thomson as manager led the explosives industry in Great Britain in organization, in safety precautions and in the invention of new processes and plant. Rintoul, naturally inventive and of remarkable manual skill, did his full share, of which the displacement process for the manufacture of nitroglycerine is an example. This process improved the manufacture of that explosive economically in that no high buildings were required to house the plant and also from the point of view of safety, as the nitroglycerine was removed (by upward displacement) from its acid mixture as soon as it had been formed and was sent at once for its preliminary washing, instead of being left to separate in bulk in an acid, and more or less dangerous, state. At this time also he was co-inventor with Robertson of a process and plant for the recovery of acetone, the solvent used in the manufacture of cordite.

Accompanying Sir Frederic Nathan to Nobel's Explosives Company (now part of Imperial Chemical Industries, Ltd.) at Ardeer in Ayrshire in 1909 as chief chemist, he became research manager there and devoted himself to the organization of the laboratories and erection of many new ones. His policy had several features which have been commended by others in like position, as for example, the provision that all chemists, whether destined for research or plant, should first undergo a thorough training in analytical chemical methods, the insistence on a good system of documentation of reports and of published work, the installation of physical methods of testing explosives and close contact with the universities. While at Ardeer he was associated with a number of patents chiefly on stabilizers for explosives, and developed a keen interest in biochemical investigations, some of which are described (with Raistrick) in the *Philosophical Transactions of the Royal Society*.

About ten years ago Rintoul was brought up to the headquarters of Imperial Chemical Industries, Ltd., as a director of its research organization, from which he maintained an active and sympathetic contact with all the company's laboratories, and came into close touch with many prominent scientific men who were working directly or indirectly in the company's interests, for it was part of his duty to administer the support given by the company to wide-spread scientific activities. In these matters he gained the respect and affection of everyone with whom he came in contact, and as representative of his firm was well known abroad, where he attended many conferences.

Rintoul was made an O.B.E. for his work in the Great War, and assisted on many committees such as the Councils of the Chemical Society and Institute of Chemistry, the Safety in Mines Research Board, the Chemistry Research Board (D.S.I.R.), the Research Committee of the Midland Railway and the British Standards Institution. When he died he was president of the Faraday Society, in the discussions of which he took much interest.

Rintoul married twice: first Lottie Edwards, by whom he had two sons and a daughter, and secondly, two years ago, Jess Isabel Robertson. (Sir) R. ROBERTSON.

ALTON EWART CLARENCE SMITH.

1887—1936.

A. E. CLARENCE SMITH was born on March 20th, 1887, at Chislehurst, a son of Sir Clarence Smith, J.P., D.L., of Wilmington Manor, Dartford. He was educated at the Leys School and at Christ's College, Cambridge. After taking first classes in the Natural Sciences

Tripos, Part I in 1908 and Part II in 1910, he returned to the University to undertake research but had to abandon this owing to ill-health. Some time later he went as a student to the Marine Biological Station at Plymouth and his interest in microscopy dates from this period. At the outbreak of war he volunteered for military service, and was given a commission in the 13th South Lancashire Regiment in September, 1914. He was gazetted Captain in 1915, but after active service in France was invalided out in 1917 with acute gastritis. He afterwards returned to work with the Effandum Company at Wolverhampton, where prior to the war he had been employed as research chemist, and where munitions of war were now being manufactured.

In 1919 he was appointed Lecturer in Physical Chemistry at University College, Southampton, a position which he occupied until his death on September 16th, 1936. At the time of his appointment the University College had just moved into its new buildings at Highfield and the planning and equipment of a laboratory for Physical Chemistry was one of his earliest tasks. At first use had to be made of one of the Army huts erected during the occupation of the College buildings as a Military Hospital, and in the transformation of this unpromising building into a laboratory for Physical Chemistry Clarence Smith showed characteristic ingenuity. Some years later a more suitable building became available and the fitting up of this as a Physico-chemical Laboratory again gave scope for his originality and mechanical skill as well as his scientific knowledge. His own research work was devoted chiefly to studies in connection with photomicrography; his publications in the *Journal* of the Photo-micrographical Society, the *Journal* of the Quekett Club and similar periodicals had given him a recognised position as a leading expert in this subject. He had recently been awarded the medal of the Royal Photographic Society and, in the opinion of one very competent judge, he was without exception the most accomplished technician in photomicrography in this country. But Clarence Smith was in the first instance a teacher. His main efforts were devoted to the building up of his young and growing department of Physical Chemistry and to maintaining the teaching of his subject at the highest possible degree of efficiency. For this task he was especially fitted by tastes and natural endowments. He had a remarkable gift for accurate speech and writing and a corresponding dislike for careless and inexact phrasing. He had read widely and always with a critical mind. He took very great pains in the preparation of his lectures, and these were extraordinarily clear and effective. He was very happy in his relations with his students, who had a warm affection and respect for him. They knew that he always gave them of his best and that he would grudge no expenditure of time or trouble to help them. By his colleagues on the staff of the University College he was held in peculiar esteem as a man obviously free from all petty jealousies and whole-heartedly working for the common good. His tact and judgment, combined as they were with an unfailing courtesy, often proved decisive factors in achieving a happy solution where difficult academic problems were involved. He was always ready to place his scientific knowledge and experience at the service of his colleagues, his wide scientific interests (which included zoology as well as physics) making it possible for him to give helpful advice in more than one branch of study.

The research work in chemistry at Southampton during the past seventeen years owes a very special debt of gratitude for his ready interest and generous help. Another aspect of Clarence Smith's contribution to the development of the University College deserves mention. He acted for a number of years as secretary to the Faculty of Science and in this capacity showed gifts of organisation of a very remarkable kind. In this work, as in everything else which he undertook, he never spared himself. His death, which occurred with tragic suddenness as the result of an illness contracted while he was enjoying one of his favourite holidays on the Broads, has deprived University College, Southampton, of one of its most able teachers and one whose personal influence was felt and greatly valued in many different phases of College life. He married in 1916 Hilda Burnet, daughter of Mr. Theodore E. Salvesen, of Carbisdale Castle, Culrain, and is survived by his wife and four children.

D. R. Boyd.

SIR RICHARD THRELFALL, G.B.E., F.R.S.

1861—1932.

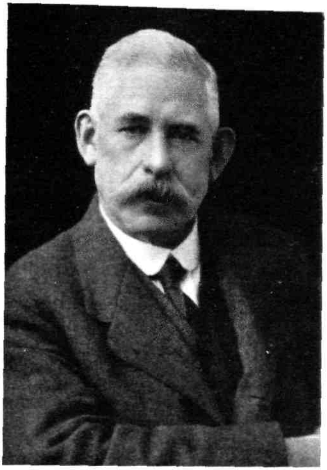
Fifty years ago when Threlfall was twenty-five there must have been few scientists in England who had never heard of him: to-day it is possible that the majority of Fellows of the Chemical Society know little about him. Yet he was one of the great men of his age: great in achievement, in character, and in his power to stimulate others to produce the best that was in them. His best work was, and still is, confidential in nature; and most of his published scientific work, although it shows ample evidence of his experimental skill, has left little obvious mark on the progress of Science. It is all the more necessary, therefore, in this short memoir, to try to preserve a true impression of a man who had an outstanding reputation among his contemporaries.

Richard Threlfall was born on August 14th, 1861, at "Hollowforth", in the village of Woodplumpton near Preston. His father had been in business in Preston as a wine merchant and was Mayor of Preston in 1855—56. His mother was his father's second wife; she had six children, two of whom died in childhood, leaving Richard the eldest. He had two brothers, one an able botanist, who was drowned near Baghdad on a botanical expedition, and the other an engineer, who also died abroad. His sister, Mrs. Ascroft, survives him.

Threlfall had few memories of his father, who died in 1870. A year before his death, he was asked by his son to help him to make a galvanic battery, but did not rise to the occasion. This lack of parental encouragement seems to have stimulated rather than deterred the boy, and from that time on Richard Threlfall taught himself to be an experimenter. While he was still young he equipped for himself a work-shop and laboratory in the garden at Hollowforth, and like many boys started experiments on explosives. Unlike most boys, however, he continued such experiments throughout his life and became one of the first authorities on the subject. He did not succeed without personal injury, for at an early age an explosion blew off the third and little fingers of his left hand as well as the top joints of the right thumb and index finger, and incidentally shattered his ambition to become a Royal Engineer. It is recorded that on the way to the hospital he insisted in having his mouth propped open by a piece of wood so that, if he should get lock-jaw, he should not be starved to death as well. It is also recorded that he continued his experiments on explosives when he went to Clifton College in January, 1873, to the satisfaction of his schoolfellows but not altogether to the approval of the masters. With what aid he could get from the village nearby he also taught himself the use of tools, and amongst other things successfully constructed a telescope, made a hydraulic ram to supply water to the garden and, at the request of his mother, fixed up a workable telephone between the garden laboratory and the house in the vain hope that occasionally he could be induced to return punctually for meals. His mother, like the mothers of many great men, had a great influence on him, and he used to speak of her not only with the deepest affection but with the greatest respect for her wisdom and judgment. From the time he made his first experiments to the end of his life, for a period of over sixty years, there were very few working days in any year when Threlfall was not to be found for some period experimenting in his laboratory.

When Threlfall first went to Clifton, Percival was the headmaster. They were great days at Clifton; he had as schoolfellows many boys who made their mark in different ways, including four future Fellows of the Royal Society. For some time he shared a study with the future Lord Haig. It is often said that one way to be great is to choose one's parents carefully; but many instances lead one to believe that it is just as important to select one's schoolfellows with equal care: or is it possible that great schoolmasters have a more permanent effect on their pupils than they are usually credited with?

Threlfall was a keen member of the Rugby fifteen at Clifton, and also a member of the shooting team. He left school in 1880, and went to Gonville and Caius College, Cambridge, with an entrance scholarship. Again he found himself with contemporaries of equal ability, one of them being a future President of the Royal Society, Sir Charles Sherrington.



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The photograph of Sir Richard Threlfall as a young man is taken from a group photographed by Dr. Alexander Scott in 1882.

In his second year at Cambridge, he produced the first automatic microtome, and by doing so made a contribution of the first importance to experimental biology. No account was published by him for nearly fifty years, when he communicated the history of this development to *Biological Reviews* (Vol. V, Oct., 1930). The history in brief is as follows:

The method of cutting sections before 1882 was to embed the specimen in paraffin and cut the sections by hand with a sharp razor. The instrument, such as it was, consisted of a glass plate with a central hole, through which a brass tube could be pushed by means of a micrometer screw. The brass tube carried a lump of paraffin on to which a piece of paraffin containing the embedded object could be melted. By this primitive method, it was impossible to get a uniform thickness of section; some sections might be three or four times as thick as others.

In May, 1882, W. H. Caldwell noticed that, if the paraffin was of the right consistence, the section adhered to the razor at the sharp edge of the blade, and did not adhere elsewhere. In cutting a second section without moving the first from the razor, the second section welded itself to the first when pushed across the razor. He happened to tell Threlfall of this observation and one of them remarked that it seemed to make the construction of a section-cutting machine a possibility. Afterwards they discussed the general ideas for a machine while on a trip to Heligoland. When Threlfall returned to Cambridge he started on the work with enthusiasm. From that time he had no help whatsoever from others. The design was completely his own, and he had the machine constructed in Professor Stuart's workshop at his own expense. He does not seem to have had any encouragement while the machine was in process of construction, indeed, the few comments he received were definitely discouraging. However, it was completed in 1883 and was a brilliant success from the first trial. Threlfall himself used it to cut an amphioxus into uniform sections about one four-thousandth of an inch thick, making a ribbon some yards long. He completed the work by developing a satisfactory method for dissolving away the paraffin and fixing the sections on to slides. Subsequently the rocking microtome was developed by Horace Darwin, but there is no doubt at all that Threlfall was the originator of the first practical machine. He records in his paper that when he was later at Strasburg, he told one of the demonstrators there about the construction of the microtome and the method of section mounting, and subsequently found a paper published in Germany giving all the information without any reference to the source from which it had been acquired.

In 1882 Threlfall took a first-class in Part 1 of the Natural Science Tripos. In the spring of the next year he took advantage of a new regulation which allowed candidates for the Science Tripos to spend a period up to one year in work abroad, and went to Strasburg to work with Fittig and Kundt from April, 1883, to the end of the semester. He always looked back to this time as one of great profit and pleasure to him. He seems to have taken a particular liking to Kundt, and the attraction was evidently mutual. He visited him in after years, and after his death referred to him in these terms in an anniversary address delivered to the Royal Society of New South Wales in 1895:

"Before all things, Kundt was what the Germans call 'gemüthlich'—a jolly fellow. His method of teaching was copious and admirable conversation in the laboratory, and there probably never was a teacher who had so strong a hold upon his pupils—a hold both of heart and head. He was a thorough German, too. His surprise at seeing me, a man who had been to Australia and actually returned, was exquisite. He was even late for lecture to celebrate the event. 'Eheu fugaces'—the least of all thy servants bids thee adieu, dear master, there is no other man like thee."

In 1884 Threlfall took a first-class in Part 2 of the Natural Science Tripos. During his undergraduate career he continued to work hard in the laboratory at home as well as at Cambridge and to read widely and untiringly. He was a member of the University Dramatic Society and once played the part of Heracles in "The Birds" of Aristophanes. The "property" club with which he was provided was too light for him to wield with verisimilitude and he insisted on having a genuine solid article, which others could hardly lift. He was a famous Rugby football player and was captain of the Cambridge team at the time of an historic incident. No full "blues" were then given except for rowing and the blues committee consisted naturally of rowing men. Threlfall renewed an application for

an award of this much coveted distinction to the Rugby team but was refused. In his characteristic manner he took matters into his own hands and ordered his team to appear in full blues against Oxford. This led to a first-class row, and to a debate at the Union at which all members of the University were allowed to be present. Sir Joseph Thomson has given a vivid account of the scene in his obituary notice of Sir Richard Threlfall published by the Royal Society :

"The room was so crowded for some time before the proceedings began that when Threlfall, on whom the hopes of the Rugby supporters rested, arrived, he could not get beyond the crowd at the back of the room, and had to be held up by some friends while he made his speech. The speakers before him delivered carefully prepared orations which smelt very much of the lamp, and left the audience quite cold. When he got up and jerked out from his uncomfortable stance one short sentence after another, full of good sense, good humour and good jokes, he soon had the house rocking with laughter and put the issue beyond doubt."

The only thing I need add to this description is that one of the friends on whose shoulders Threlfall precariously rested was Sir Joseph Thomson himself.

It is not difficult to recapture something of the impression that Threlfall made at this time of his life. He must have been quite out of the ordinary. His love of country life, and his skill at sport as well as at games, had developed a naturally powerful frame. He was a good shot with gun and rifle, and a good fisherman and remained so for the rest of his life. He had an unusually wide range of interests. He was passionately fond of flowers, a taste which he had probably acquired first on his visit to Switzerland as a boy when recovering from the accident to his hands. He had, indeed, a tremendous zest for life, which he seems to have communicated to all with whom he came in contact. He had too a full measure of that uncommon quality called commonsense, which shone in his speech and in his actions. After he had taken his degree, when he was in his fifth year at Cambridge, he took some pupils at Caius and also demonstrated in the Cavendish, and in the Caius laboratory under Pattison Muir. One of his first pupils was W. B. Hardy. Here is a description of the first interview :

"In the room I found a rather thick-set figure with a strong face and clad in a B.A. gown. Threlfall was then the most influential person in the undergraduate life of the College. He was, I think, the senior bachelor, and the gulf between the senior bachelor and a freshman is, as everyone knows, more awe-inspiring than that between the latter and the Master; the Master is merely someone unknown in the clouds.

"My first lesson in physics from Threlfall began, as might be expected, by a totally unexpected attack. 'What is a yard?' he asked. Now, no teacher of physics at school had ever asked me such a silly and embarrassing question. A yard was a thing one took for granted. I blundered along with some sort of reply only to be cut short with : 'A yard is neither more nor less than the distance between two marks on a certain rod of platinum.' And from that, to me, new and rather staggering information he passed to the relation between measures and things measured. It was his way through life to ask the question, obvious when asked, which set of people wondering whether they had not committed the nursery trick of mankind—picking up the wrong measuring rod."

Threlfall had no opportunity for a Fellowship, which in those days were few and far between. No easy road to an academic career existed by way of postgraduate scholarships, or studentships for training in research : but then Threlfall did not need a training in research ; he had trained himself, and only needed the encouragement and inspiration of others. There is a paper of his on the theory of explosions published in the *Philosophical Magazine* for March, 1886, when he was not quite twenty-five, which gives a clear impression of his capacity and maturity. In this research he set himself to examine how the shock of an explosion was transmitted under water, and to test the existing theories of the mechanism by which one explosive might be exploded by the detonation of another at a distance. He carried out a series of experiments in his own garden at home, detonating small charges of fulminate of mercury in a wooden tank measuring about a yard each way, filled with water, and measuring the effects with homemade pressure gauges. The interest of the paper lies now not so much in the results obtained, although they were novel at the time, as in the

ingenious and inexpensive methods used, and in the evidence it gives of Threlfall's mastery of experimental work, confidence in his own powers, and ability to express himself forcibly. While at Cambridge during these years he also collaborated with the then young Professor J. J. Thomson in various researches, including one on the effect of electrical discharges through nitrogen at low pressure. They reached the tentative conclusion that an allotropic form of nitrogen was formed under certain conditions. A few years afterwards, in 1889, Threlfall returned to this work, and showed that what actually happened was that an unstable compound of nitrogen was formed with the mercury present in the apparatus. It took him over two years to settle the point and his paper on the subject (*Phil. Mag.*, 1893, **35**, 1) is devoted largely to a detailed description of his efforts to prepare pure nitrogen from various sources. It is of interest to note that had he had occasion, at this time, to measure the density of his samples of nitrogen, he might possibly have anticipated the discovery of argon by Lord Rayleigh in 1894.

In 1886 Threlfall was offered and accepted the Professorship of Physics in Sydney University. He took Sydney by storm. Even in these days in England, when no one is surprised that a distinguished Professor should be an ordinary-looking and even a capable individual, the appointment of a young man of the age of twenty-five, better known to the outside world for his athletic fame than for his intellectual attainments, would excite some comment. But fifty years ago in Australia, where brawn was undoubtedly considered more important than brain, the appearance of such a man was greeted with enthusiasm. A correspondent to *The Times* at the time of Threlfall's death wrote of the "deep impression Threlfall's personality made upon the students of the University of Sydney and the far-reaching influence he exerted. A professor who not only took an interest in football but actually played with the University team was a new phenomenon. But Threlfall did much more on the football field than give practical instruction in Rugby tactics. Although his vocabulary was regarded as adequate, even for Australia, he would not tolerate any liberties. He taught the team many lessons in social practice, which were not wholly unnecessary.

"It was, however, as a teacher of physics that his dominating personality exerted most influence in Australia. He gave many undergraduates a new conception of the methods and meaning of science. His first lecture is deeply impressed upon the writer's memory, his experiments to demonstrate smoke vortices and to interpret J. J. Thomson's theory of matter and energy, his impressive warning that science did not teach dogmas but should be ever alert to modify its theories in adaptation to new facts revealed by experiment. No less surprising to many of us, who until then had imagined that science had a definite doctrine to inculcate, was his advice to read Draper's 'Conflict between Religion and Science,' and learn to distinguish between dogma and the open mind. It would be difficult to assess the effects his robust personality exerted in Australia by inculcating the true scientific attitude.

"His manner with students this personal experience will illuminate. The writer was awarded the only University prize in physics. Threlfall sent for him and said, 'Don't run away with the idea you know anything of physics: you were simply the least unsatisfactory of a poor lot.'"

Threlfall arrived in Sydney to find no physics laboratory and threatened to go back unless one was provided. At first he was given a few unsuitable rooms, and vague promises of better things; but nothing could stop him from experimenting, and he soon made friends with the naval and military authorities, and with their help, and with the collaboration of J. F. Adair, then demonstrator of physics in the University, started towards the end of 1886 on a closer investigation of the alleged "explosion by influence." He finally disposed of this phenomenon by proving that it did not exist, and went on to measure the velocity of transmission of the shock of explosions through water. He succeeded in showing that the velocity was greater than that of sound, and increased substantially with the size of the explosive charge. A full description of the work was published in the *Proceedings* of the Royal Society (1889, **46**, 496).

Meanwhile his pertinacity in pressing for a suitable laboratory, and his capacity for making friends with everyone, had their reward. In Sir Joseph Thomson's words:

"One night the Prime Minister came up to him in the club and said 'Dick, I have done the square thing by you at last. I've put your laboratory on the estimates. We've just been beaten on a division and are resigning to-morrow so that the other fellows will have to pay.'"

The vote in the first place was for £8000, afterwards increased to £13,000, which probably corresponded to an expenditure of about £7000 in England. The building was begun in February, 1887, and handed over in June, 1888. There is an interesting description of it, written by Threlfall, in the *Proceedings* of the Australasian Association for the Advancement of Science, in 1888. One part of this description is worth quoting because, although written nearly fifty years ago, it seems singularly apposite at the present time, and shows Threlfall's attitude towards experimental work :

"In my experience experimenting is neither more nor less than doing a number of small jobs: one's thoughts are always far ahead of the particular part of an experiment one may be engaged on ; and hence the quicker we can make the satisfaction of our experimental needs, the more efficient will our work become. It is for this reason among others that I prefer a good big place to work in—a place where every part of an experiment can be done—and where loss of time through running about shall be reduced to a minimum. Even for purposes of instruction I utterly fail to see the advantages arising from the use of antiquated or inefficient appliances. Experimental facility can I believe be acquired just as well by working with good tools as with bad ones : and the amount of ground got over is greater, the greater the efficiency of the appliances. Of course I do not mean to say that students should be furnished with all their experiments ready set up—this I believe to be a great mistake—I think the best work for students is the most difficult and tiresome, and that requiring the greatest accuracy—but why should we add to that the annoyance of insufficient or make-shift appliances? I am of course talking of physical work—in such cases as Mineralogy—where the student will in after times have to work with meagre instrumental assistance, handiness and a power of adaptation of things to want, are the most valuable possessions that education can furnish : so that much apparatus may in this case be a bad thing. But this is not to any extent the case with Physics. It is true of course that many great men have performed great experimental feats with the simplest of apparatus; but the contemplation of such cases has always stirred within me some feeling of regret that the means were so inadequate, and this has quickly overpowered the feeling of delight in the results attained. On the whole I conceive that the work done in a Physical Laboratory is not unlike the work done in an instrument maker's shop; and that both should be constructed on the same principle of time-saving."

This, it should be noted, is the opinion of a man quite outstanding in his experimental ability.

For the next eleven years, with the help of members of his staff, and research assistants, Threlfall was very busy with a variety of researches. That on the effects of electrical discharges through pure nitrogen has already been mentioned. His study of dielectrics extended over many years, in the course of which he was led to examine the Clark cell as a source of small standard currents, to develop methods for the measurement of high specific resistances, and to design and construct a galvanometer to measure currents as low as 10^{-12} ampère. He made an elaborate series of researches on the preparation of pure sulphur, and on its electrical properties. He was quick to realise the importance of the discovery in 1889 by C. V. Boys of the properties of fine quartz threads, repeated and extended the method of production invented by Boys, and made exact measurements of the elastic constants of the threads. He made use of the quartz thread in the development of an instrument for the comparison of the force of gravity at different places. With this instrument he and Pollock, who eventually succeeded him as Professor, travelled over 6000 miles in Australia and Tasmania, taking observations. In spite of rough usage, only one quartz thread was broken, and one lasted for over 4500 miles. The accuracy of measurement by this instrument proved to be as high as 1 part in 500,000. An account of the work was published in the *Philosophical Transactions* in 1900 (193, *A*, 215), and Threlfall exhibited the instrument at the meeting of the British Association in Dover in 1898. It was then returned to Australia but remained stored in a cellar for twenty-seven years,

when it was sent back to England. On examination it was found that the quartz fibre and its suspension were undamaged, but the rest of the apparatus was in such bad order that Threlfall had it entirely reconstructed. With the help of Dawson he then used it for the comparison of gravity at the National Physical Laboratory, and at Kew, and gave an account of this work to the Royal Society a few months before his death.

In 1898 he published his book on "Laboratory Arts." He seems to have had some difficulty in finding a publisher at first, but the book was a great success, and "go to Threlfall" was advice frequently given and acted upon. It is a storehouse of valuable information on laboratory technique, and, with a few trivial exceptions, all the directions and suggestions it contains are derived from the author's own personal experience. All the illustrations in this book were drawn by his wife. Towards the close of his life he was engaged on, but did not finish, a new edition of this work.

In 1890 he returned on holiday to England, and paid a visit to Professor Van der Waals in Holland, with whom he discussed certain difficulties in the latter's famous paper of the continuity of the liquid and gaseous states of matter, an English translation of which by Threlfall and Adair was later published as a Physical Memoir. Threlfall used to say that the discussion with Van der Waals was conducted by an exchange of notes written in dog-Latin.

He married in 1890 Evelyn Agnes Baird, who was one of six talented daughters of John Forster and Emily Jane Baird of Bowmont Hill in Northumberland. One of Lady Threlfall's sisters was well known as Dorothea Baird, who married H. B. Irving, and another married A. L. Smith, afterwards Master of Balliol College, Oxford. Lady Threlfall was an unusually clever woman; she had a most retentive memory and an "extensive and peculiar" acquaintance with the works of Dickens. She published two volumes of poems: Starlight Songs (1895), and The Shore of Dreams (1907). She died in 1929, when Sir Richard was returning from Japan where he represented the government at the World Power Conference. Four sons and two daughters survive them.

The general impression left by a study of Threlfall's scientific work in Australia is that he continually added to experimental knowledge without making such a contribution to scientific progress as might have been expected from a man of his remarkable ability. It would be fair to say that he was really too interested in the details of experimental work, and the fact that the difficulties of some experiments were too great for the immediate end in view never led him to attack anything more promising; on the contrary the bigger the experimental difficulties the more he seemed to be stimulated to overcome them. These are pre-eminently the qualities required in applied Science, but do not necessarily lead to notable success in pure Science. Threlfall enjoyed the frontal attack, and did not believe in inspiration although perhaps some of his own work owed more to inspiration and less to exact scientific reasoning than he imagined. In an address to the Australasian Association for the Advancement of Science in 1895, he referred to the discovery of argon, and added:

"I cannot close this brief notice without directing your attention to the magnificent triumph which this discovery has obtained for the method of enquiry by means of prolonged, laborious, and exact measurement as opposed to the method of happy inspiration. Contrary to the popular idea, the vast majority of discoveries have been made by the methods employed by Lord Rayleigh, of which the essence is that no obscurity, however small, is to be passed over until it is completely sifted."

It was typical of Threlfall that he could not leave any obscurity alone, and it was unfortunate that none of the obscurities to which he gave so large a share of attention and examined with so much skill led to any outstanding advance in Science.

In the midst of his scientific work he found time to carry out a fair amount of work as a consultant; an experience which was valuable to him later on. He was also president of the Royal Commission of the Spontaneous Combustion of Coal. This Commission was appointed in 1896 and issued a report of the first importance a year later. He was President of section A of the Australasian Association in 1889/1890, and delivered an address on "The Present State of Electrical Knowledge" in the course of which, after discussing the work of Maxwell and Hertz on electromagnetic waves, and describing methods for

their detection, he indulged in a prophecy which has since been amply justified. "If it be permissible to prophesy wildly, we may see in this observation the germ of a great future development." He was also President of the Royal Society of New South Wales in 1895. It need hardly be added that during his stay in Australia Threlfall found time to see much of the country, including New Zealand and Tasmania, and to indulge in his love for outdoor sports.

In spite of his manifold activities, his friendships and his affection for the place, Threlfall never felt quite secure in his position in Australia. Seven years after he had got his laboratory, in a reference to the work of Helmholtz, who had recently died, he said that Helmholtz "recognised that in physical science stagnation means retrogression, and that the man who has not the curiosity to attempt to widen our common knowledge is not fit to set himself up as a teacher, nor are the pupils of such a man likely to receive any lasting benefit. If Helmholtz's words, so fruitful first through Germany and France, and then through England and America, could find even at this late date some echo in the Colony, we might be gradually educated up to seeing that the commercial value of a teacher is not to be measured by the number of hours of lecture that can be dragged out of him, nor is a laboratory to be regarded as an expensive luxury to be blown away at the first breath of retrenchment." He was out of touch with many of his scientific friends, the nearest being W. H. Bragg at Adelaide. His wife's health suffered in the climate of Sydney, and he had to think of the problems of a young family now fast growing up. When he came back to England for a visit in 1899 it was with the intention of finding work at home, but no suitable Professorship seemed likely to be vacant in the near future, and after full consideration, he decided to accept an offer to join the well-known firm of Chemical Manufacturers—Messrs. Albright & Wilson in Birmingham. That the decision was a wise one there can be no doubt. The particular range of activities of Messrs. Albright & Wilson was exactly suited to Threlfall's interests; applied electro-chemistry was a subject which exercised to the full his profound knowledge of physics and chemistry and his ability as an engineer. He settled down in Birmingham in 1899, and for fifteen years devoted himself entirely to the affairs of the firm; in his own words he became: "a type of man wholly immersed in provincial business." As it happened he saw little of his scientific friends during this period, visiting London and Cambridge not more than two or three times a year: and apart from being a member of the Council of Birmingham University, of one of the Committees which led to the formation of the Imperial College of Science and Technology, and of the Royal Society Committee on Electrical Units, he did little outside work. On the other hand, fifteen years of strenuous technical research at Oldbury gave him a unique knowledge of chemical and physical methods as applied to manufacture. He worked out a method for the electrolytic manufacture of sodium chlorate which was operated successfully on a large scale at Niagara Falls. He also developed a method for the electrolytic production of zinc, which was a magnificent triumph over experimental difficulties, but unfortunately was not adopted in the end, as it proved for various reasons to be uneconomic. The only advantage of this decision was that it gave him the opportunity to publish an account of the work in the *Journal* of the Society of Chemical Industry in July, 1929, on the occasion when he was given the Gold Medal of the Society. A remark in this paper is characteristic of him. After referring to the formidable experimental difficulties, he says "However, I decided in the end that such difficulties as might arise could probably be overcome by steady work and engineering." He also introduced many improvements in the production of phosphorus by the electric furnace and installed a large gas engine plant to which reference will be made later. No details of Threlfall's work during this period can be published other than those which have already appeared in various journals. In an address on some problems of electrochemistry to the Birmingham local centre of the Institution of Electrical Engineers in 1905 Threlfall said:

"Reticence is a tradition of the chemical industry, and the introduction of processes based on electrochemical operations has, if anything, increased the habit of, as well as the necessity for, uncommunicativeness. The manufacturer of machinery has really no secret except his organisation—the machines he sends out speak more or less for them-

selves, and render it futile to endeavour to conceal matters of design or construction. The products of a chemical works, however, do not necessarily indicate their mode of manufacture. . . . It would require very expert knowledge to decide whether a sample of chlorate of potash was manufactured electrolytically or from chlorine."

One result of this reticence was that much of Threlfall's unique knowledge of electrochemistry died with him; which is perhaps as unfortunate in the long run for the progress of industry as it is for the advancement of science. Threlfall himself was apt to be somewhat contemptuous of the academic electrochemist; he used to say that many of the statements in text books on electrochemistry were misleading if not absolutely wrong.

The nature of his work made it necessary for Threlfall to be concerned in the production of electrical power on a large scale at Oldbury. For various good technical reasons, it was decided to install a gas engine plant, the only suitable engines for the purpose being obtainable, at the time, in Germany. In the course of his work on the design and general arrangement of the plant, Threlfall was led to study the efficiency of electrical generators in 1901. The testing of alternators was then in a very primitive state and the uncertainty of the results of measurement of efficiency was a serious difficulty to the manufacturer and users of large alternators. In some installations it was practically impossible, owing to constructional peculiarities, to measure the brake horse-power developed by an engine under running conditions. Threlfall got over the difficulties in a most ingenious way, by enclosing the alternators in a non-conducting casing, pumping air through the system at a measured rate, and ascertaining the rise of temperature of the air on entering and leaving the system. He published a full account of this work in the *Journal* of Proceedings of the Institution of Electrical Engineers in 1903. It gave rise to considerable interest and discussion, the general opinion of engineers being that it was the kind of a thing only a physicist could do. Threlfall pointed out in answer to the discussion that the method was quite amenable for use by anyone who was accustomed to exact measurement, and that no other sufficiently exact method appeared to be immediately available for users. The method involved exact measurement of the velocity of air in the ducts, and for this and other reasons Threlfall spent some time on the theory and use of the Pitot tube method. He published the results of these researches in the *Proceedings* of the Institution of Mechanical Engineers, February, 1904: the paper and discussion are of interest in showing Threlfall's combination of scientific knowledge and technical judgment. For instance he makes the following characteristic remark:

"Professor Unwin's remarks on matters of theory were based on the hydrodynamics of frictionless fluids; no doubt the author's treatment was lamentably defective, but it had the merit of not taking for granted that producer gas would behave so nearly like a frictionless fluid that calculations involving large sums of money could be safely based on that hypothesis."

Threlfall also spent some time on the development of apparatus to withstand high pressures and temperatures, and used it to examine the possibility of producing diamonds from carbon, a subject which created much interest at the time. It was not altogether without value for his own purpose, because he was studying the properties of carbon for other reasons.

In 1914, just before the outbreak of war, the large gas engine plant was completed at Oldbury. For fifteen years Threlfall had worked in some obscurity, so much so that when the war broke out it seems to have occurred to no one at once to enlist his help in the many technical problems, the solution of which immediately became urgent. He offered his services to the Admiralty and to the War Office, but was told that he was too old. He was then fifty-three. It was only through his own enterprise that he became eventually closely concerned with national affairs. About the end of October, 1914, he read a statement subsequently shown to be untrue, that the Germans were using a non-inflammable gas in their air-ships. Knowing the German competence for big engineering projects, he wondered whether it was within the bounds of possibility that they had got a practical source of helium from gas wells or coal mines. On looking through the available literature, he found the record of a gas well near Hamburg with a relatively high percentage of helium. He brought this to the atten-

tion of the Admiralty and was asked to investigate the matter further. He then found a record in the transactions of the American Chemical Society to the effect that a gas well in Kansas had given upwards of two per cent. of helium. At his own expense he arranged for one of his collaborators at the Niagara Falls branch of Messrs. Albright & Wilson to collect samples from the well and to analyse them. The analysis confirmed the original statement, and subsequently samples were sent home and analysed by Sir William Ramsay, who got confirmatory results. Threlfall then worked out a general scheme for producing the gas in quantity and arranged for other experiments on the diffusion of helium through balloon fabric. For very good reasons it was decided not to proceed with the scheme at the time, but a grant was made by the Admiralty to Professor MacLennan to enable him carry out further experimental work in Toronto. Subsequently, as is well known, helium was produced on a large scale in America, and Threlfall's predictions were fulfilled.

As a result of this work on helium, he was invited by the Admiralty to serve on a committee of the Naval Board of Invention and Research which had been formed in 1915. Although his work was at first confined to matters arising from the helium projects, his services were soon enlisted in other directions, and he became very closely concerned with a variety of naval problems. From then onwards his war work rapidly extended. No details of it can be given, but it is no secret that he was the originator of phosphorus bombs and of methods of production of smoke screens, which were used successfully on an enormous scale. On one occasion he was asked to produce some special bombs in a hurry for use in France, and he and his staff, working day and night, designed, tested, manufactured, and sent off one thousand of the bombs required within a fortnight. They arrived in time to be used with devastating effect for the destruction of enemy kite balloons before the Battle of the Somme.

After the War he wrote a short confidential account of his work and experiences, including impressions of the principal people he met. Those who knew Threlfall well can imagine that these notes make interesting and entertaining reading, and will also readily accept the statement that they are not for present publication.

All this war work, disturbing as it must have been at first to the normal course of his life, was of great advantage to Threlfall. It widened his interests, gave him greater scope for his powers, and caused him eventually to be concerned with national work of a permanent, as well as of a temporary, importance. The lack of scientific preparation that was so obvious in 1914 led the Government to set up in 1915 an Advisory Council for Scientific and Industrial Research, not only for war purposes, but with the more long-sighted view that it would be necessary for the promotion of science and industry after the War. Threlfall was one of the original members of this Council and served continuously for a period of ten years, after which he continued to be associated with the Department of Scientific and Industrial Research until his death. He enjoyed this period of his life as much as any. He threw himself with the greatest enthusiasm into the plans of the new organisation and was undoubtedly the hardest worked, and the hardest working, of all the distinguished members of the Advisory Council. He took an immense amount of pains; nothing was too great a trouble for him to do. He believed in the work, he enjoyed the discussions, and being a man with so great a capacity for friendship, he enjoyed also the opportunity of renewing his old friendships and making new ones. His criticism could certainly be trenchant, and his strongly individualistic temperament inclined him at times to doubt the wisdom of some of the plans for organising Industrial Research. I can see him now, sitting at the Council table with a sardonic gleam in his eye, while someone over-elaborated a "scheme of research." Nevertheless, he showed his essentially scientific habit of mind by always being prepared to make a reasonable experiment in administration as well as in science. His influence on the Department can hardly be over-emphasised. Other great industrialists have been associated with the Advisory Council, but none who had so wide a range of knowledge and experience of the academic and industrial worlds as Threlfall, and none with quite his sense of proportion. He combined the practical qualities of an engineer with a profound and sincere belief in the value of research, not only for its own sake, but as a necessary preliminary to industrial progress.

One instance of his foresight may be given. When he became Chairman of the Fuel

Research Board in succession to Sir George Beilby, he strongly urged the necessity for research on the design of industrial furnaces. In his view the design of furnaces had always been empirical; and although the process of trial and error over a number of years had often led to results in industry which would be difficult to improve upon substantially by scientific research, it had failed in this case, and large sums of money were wasted annually because there were no sound principles of design. He maintained that no substantial advance would be made until much more knowledge was available on the transfer of heat from hot gases; and he put forward a plan for the scientific study of the problem, with the warning that it might be many years before practical results emerged. His advice was followed; and a small staff worked under his general guidance. His predictions have been entirely fulfilled; our knowledge of the subject has been greatly extended, and has already been applied with success to large-scale operations. Threlfall was also responsible for starting the Government Chemical Research Laboratory at Teddington, and gave much of his time to its design and equipment. He was Chairman of the Chemistry Research Board, and acted as part-time Director of chemical research until the appointment of Sir Gilbert Morgan.

It is of interest that in 1919 he was asked whether he would allow his name to go forward for the Directorship of the National Physical Laboratory in succession to Sir Richard Glazebrook. After serious consideration he decided against this; he was certainly wise in doing so, for at the National Physical Laboratory he would have had little time for the individual work which was part of his very nature, and the large amount of administrative work which is so unavoidably associated with the direction of a big government research laboratory would have proved irksome to him. He remained at Birmingham, his main work for the firm after the War being the improvement of methods for the manufacture of carbon tetrachloride, the manufacture of glycerophosphates, and the manufacture of carbon disulphide. The gas engine plant which operated with success for the whole of the War period was shut down and sold as scrap in 1919, because it was no longer useful from a commercial point of view. Threlfall parted with great regret from the machinery to which he had devoted many years of brilliant work; but that is one of the drawbacks of industrial life; the best work often bears fruit for too short a time.

Threlfall was elected a Fellow of the Royal Society in 1899 and an Honorary Fellow of Gonville and Caius College in 1905. He was also created K.B.E. in 1917, and G.B.E. in 1927. He was given an honorary degree of D.Sc. by Manchester University in 1919, and was made an honorary Associate of the Manchester School of Technology in September, 1930. As has already been mentioned, he received the Gold Medal of the Society of Chemical Industry in 1929. After some months of gradually failing health, he died on July 10th, 1932, at Edgbaston.

Threlfall's life in retrospect seems to be divided into three quite distinct phases. The first covers his academic career, during which, starting from nothing, he built up a school of experimental Physics in Sydney, and succeeded in leaving behind him a spirit of research that has never deserted the University. He went to Australia at a time when Science was almost completely neglected; and that it is now a country where, in proportion to the size of the population, Science plays as great a part in national affairs as in any other country, is surely due in no small measure to his lasting example and inspiration. He then abandoned his purely scientific work to become a comparatively unknown, but outstandingly successful chemical engineer and manufacturer. In the third and final phase of his life, in the fullness of his powers, with years of hard-won experience behind him, and with inexhaustible energy, he rendered service of incalculable benefit to his country. In all these phases of his life he excelled. "And yet," his life-long friend Sir W. Hardy wrote in the Caian for 1933, "to me, knowing his great gifts, those successes never seemed enough. With his gifts of character, of mind, and of speech he might have been, and somehow he ought to have been, a great public figure. He was far and away bigger and wiser than most of the public men I have met. The answer as I see it is simply that he did not want to be in the limelight. His ambitions were of the homely friendly sort. The judgment of his scientific friends of the Royal Society was a thing which mattered greatly to him, and in the main he just did the job that came along."

H. T. Tizard.

34. *The Structure of Xanthone and the Orientation of its α- and β-Dinitro-derivatives.*

By C. G. Le Fèvre and R. J. W. Le Fèvre.

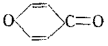
Xanthone (I) when nitrated is converted into a mixture of α- and β-dinitro-derivatives, m. p.'s 190° and 260—262° respectively (Perkin, J., 1883, **43**, 193; Richter, *J. pr. Chem.*, 1883, **28**, 292; Graebe, *Annalen*, 1889, **254**, 286). The latter was formulated as the 2 : 7-dinitro-compound by Baeyer (*Annalen*, 1910, **372**, 138), since the dimethoxyxanthone, m. p. 180°, obtained by successive reduction, diazotisation, decomposition, and methylation, appeared to be identical with a substance synthesised from *o*-chloro-*m*-methoxybenzoic acid and quinol monomethyl ether. Le Fèvre (J., 1928, 3249) showed that α- as well as β-dinitroxanthone readily underwent hydrolytic scission by boiling piperidine, and inferred that in both compounds the nitro-groups are in positions ortho or para to the oxygen atom. The structure of the dibromoxanthone, m. p. 212°, formed by the action of bromine in acetic acid containing iodine (Dhar, J., 1916, **109**, 745), is a related question, because this compound and α- and β-dinitroxanthone, when heated with bromine in a sealed tube, all form the same (unoriented) tetrabromoxanthone.

(I.)

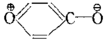
In this paper we record dipole-moment determinations on xanthone, its dibromo-, and its two dinitro-derivatives, and discuss their bearing *inter alia* on the above points. From the data tabulated later, the following results are obtained:

Substance.	Total polarisation, c.c.	Orientation polarisation, c.c.	Dipole moment, D.
Xanthone	257	200	3·11
Dibromoxanthone	421	348	4·10
α-Dinitroxanthone	253	183	2·98
β-Dinitroxanthone	747	677	5·72

Discussion.—The moment obtained for xanthone (3·11) is unexpectedly high, for by simple vector addition it should be about 1·9 (diphenyl ether and benzophenone having moments of *ca.* 1·1 and 3·0 respectively); in this particular the result recalls Hunter and Partington's observation (J., 1933, 87) that the related dimethyl- and diphenyl-γ-pyrones have moments which exceed their calculated values by 1·37 and 1·84 units. Sutton (*Trans. Faraday Soc.*, 1934, **30**, 801) considers that this exaltation arises from resonance between

(II.) 

$\mu \doteqdot 1{\cdot}9$.

 (III.)

$\mu \doteqdot 21$.

the ordinary γ-pyrone structure (II) and an excited form (III). An explanation of the present results on these lines alone would require that xanthone should possess about 10% of the character of the fully dipolar form (III). This does not seem to be the case, since it lacks the typical reactivity of the γ-pyrones, which (*e.g.*, in the 1 : 5-addition of methyl iodide or the Grignard reagent) frequently implies a facile polarisability towards (III).

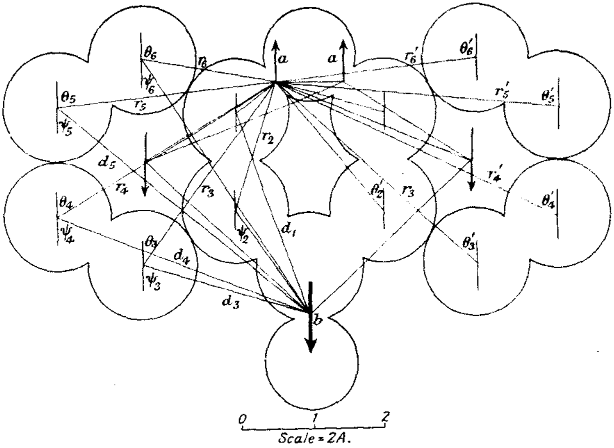
More probably the observed dipole moments of these substances arise as much from intramolecular electrostatic induction processes as from mesomerism.

An attempt to estimate these contributions in the case of xanthone will be described in detail, the accompanying scale drawing serving as a basis for the calculation. The assumption has been made that the central ring has the γ-pyrone structure; the attached aromatic nuclei accordingly correspond to one of the Kekulé forms. Evidence for this is discussed later in this paper. The double and single bond lengths used are 1·32 and 1·52 A. respectively, and the radius of oxygen 0·66 A.

The method involves the calculation and algebraical summation of the various fractional moments (μ_x) induced by the principal moments parallel to the O–CO axis. One requires,

therefore, various distances and angles; these are obtained accurately enough from the diagram. (It is noteworthy that they are not greatly different for a model in which the aromatic rings are regular hexagons with benzenoid internuclear distances and the oxygen and ketonic valency angles of the order 120°.)

The general equation for the induced moment in a medium of dielectric constant unity is $\mu_x = \alpha\mu(3\cos^2\theta - 1)/r^3$, in which α is the polarisability at a point r Å. from the seat of the inducing doublet (considered as the point of contact of the two atoms composing the polar link), and θ is the angle between r and the vertical (O–CO) direction. The link moments adopted have been: C–O, 0·9; C=O, 2·5 (Sidgwick, "The Covalent Link in Chemistry," 1933, 153). We have further assumed that the radius of carbonyl carbon equals that of carbon doubly linked to carbon; this is not unreasonable, since the chemistry of the ketone group indicates that the carbon definitely tends to be electrically positive, and elements as kations have smaller radii than when linked to other



atoms by bonds of low polarity. This simplifies the calculation, because the upward component of each ether link (a) therefore becomes 0·9 cos 52·5°. The total vertical moment due to the ethereal oxygen and acting against the CO moment (b) is twice this, *viz.*, 1·10. Each of these three components will induce moments (μ_x) in the various polarisable parts of the molecule. Only those lying in directions parallel to the vertical need be computed, however, since those at right angles are in symmetrically opposed pairs and therefore mutually cancel in the resultant.

In similar calculations for certain diphenyl compounds (*J.*, 1936, 1130) we considered the polarisability of benzene in its plane as effectively situated at the mass centre.* It might, however, be urged that this assumption is only permissible when the benzene ring is several Ångstrom units distant from the primary dipoles. In the molecule under consideration, the latter are directly attached to the rings and the induced dipoles should vary markedly in sign and magnitude on each of the carbon atoms. These have, therefore, been

* If this is done in the present case, we find (taking $\alpha = 1·24 \times 10^{-23}$ e.s.u.; Stuart and Volkmann, *Ann. Physik*, 1933, **18**, 121) the resultant calculated induced moment to be −1·68, *i.e.*, 0·4 lower than that obtained by the more detailed calculation.

calculated separately. The polarisabilities of the carbon atoms and of the CH units have been taken as the same, *viz.*, $2\cdot05 \times 10^{-24}$ e.s.u., and have been located at the centres of the carbon atoms. The results and the data upon which they are based are set out below. The distances from the point of action of each of the C–O dipoles to the centres of the carbon atoms in the nearer ring are r_1, r_2, etc., and to the corresponding carbon atoms of the more distant ring, r_1', r_2', etc. The angles which these lines make with the vertical are θ_1, θ_2, . . . , θ_1', θ_2' . . . etc., respectively. The corresponding values for the case of the ketonic dipole are d_1, d_2, d_3 . . . , and ψ_1, ψ_2, ψ_3 . . . , etc. As far as possible, the data are shown in the diagram.

r_2	$1\cdot8_6$	θ_2	17°	μ_{x2}	$+0\cdot3_6$	$r_{1'}$	$1\cdot5_8$	$\theta_{1'}$	75°	$\mu_{x1'}$	$-0\cdot2_3$
r_3	$3\cdot1_2$	θ_3	37°	μ_{x3}	$+0\cdot0_3$	$r_{2'}$	$2\cdot3_8$	$\theta_{2'}$	41°	$\mu_{x2'}$	$+0\cdot0_6$
r_4	$3\cdot5_5$	θ_4	59°	μ_{x4}	$-0\cdot0_1$	$r_{3'}$	$3\cdot8_5$	$\theta_{3'}$	49°	$\mu_{x3'}$	$+0\cdot0_6$
r_5	$3\cdot0_0$	θ_5	85°	μ_{x5}	$-0\cdot0_4$	$r_{4'}$	$4\cdot4_9$	$\theta_{4'}$	65°	$\mu_{x4'}$	$-0\cdot0_1$
r_6	$1\cdot9_0$	θ_6	100°	μ_{x6}	$-0\cdot1_5$	$r_{5'}$	$4\cdot0_2$	$\theta_{5'}$	86°	$\mu_{x5'}$	$-0\cdot0_2$
						$r_{6'}$	$2\cdot8_5$	$\theta_{6'}$	96°	$\mu_{x6'}$	$-0\cdot0_5$
d_1	$3\cdot0_6$	ψ_1	20°	$\mu_{x1''}$	$-0\cdot3_2$	d_4	$3\cdot7_6$	ψ_4	69°	$\mu_{x4''}$	$+0\cdot0_6$
d_2	$1\cdot8_0$	ψ_2	36°	$\mu_{x2''}$	$-0\cdot8_5$	d_5	$4\cdot5_5$	ψ_5	51°	$\mu_{x5''}$	$-0\cdot0_1$
d_3	$2\cdot4_5$	ψ_3	73°	$\mu_{x3''}$	$+0\cdot2_5$	d_6	$4\cdot2_4$	ψ_6	33°	$\mu_{x6''}$	$-0\cdot0_8$

In addition there are the effects of the ketonic group on the ethereal oxygen and *vice versa* to be considered. From the atom refractions (Na line) of carbon, carbonyl oxygen, and ethereal oxygen (2·418, 2·211, 1·643), the respective average polarisabilities are calculable as 0·09, 0·09, and $0\cdot07 \times 10^{-23}$. By taking the appropriate distances from the diagram, *it is found that the interaction between the ethereal linkages and the carbon and the oxygen* of the carbonyl group causes induction of + 0·11 and + 0·03, and the effect of the ketonic radical on the oxygen atom induces − 0·08 on the latter.

When the last results are added to $2\Sigma\alpha\mu(3\cos^2\theta - 1)/r^3$ (from the above tables) a resultant of −2·08 units is obtained. The *actual* induced resultant moment will, however, be $(\epsilon + 2)/3\epsilon$ times less than this, ϵ being the dielectric constant of the internuclear space. The order of ϵ should be derivable from measurements of the rate of variation of the dielectric constant of benzene under increasingly high pressures, *i.e.*, when the internuclear space is diminishing. The limiting value should be the quantity required in our calculation.

Ortvay (*Ann. Physik*, 1911, **36**, 14) found that, for several liquids, dielectric constant and pressure were connected by a quadratic relation: $\epsilon_p = \epsilon_0(1 + \alpha p + \beta p^2)$, where $\epsilon_p - \epsilon_0$ is the dielectric constant change for a pressure increase of p kg./cm.^{2}. From this equation the pressure at which ϵ_p becomes constant is $-\alpha/2\beta$, and since for benzene $\alpha.10^4 = 0\cdot603$ and $-\beta.10^7 = 0\cdot164$, the maximum value of the dielectric constant at 25° is $2\cdot273 \times 1\cdot055 = 2\cdot40$. Adopting the Clausius–Mosotti model, therefore, we estimate that the induction in the xanthone molecule should be reduced by 4·4/7·2. It accordingly becomes − 1·16 units.

Conclusions.—The observed dipole moment of xanthone ($-3\cdot1_1$) can be considered to arise from the vectorial addition of (*a*) the bond moments (+ 1·1 − 2·5), (*b*) the induced moments ($-1\cdot1_6$), and (*c*) a "mesomeric" moment ($0\cdot5_5$). The smallness of the last indicates that a form containing the pyrone unit as in (III) can only make *ca.* 3% contribution to the real structure.

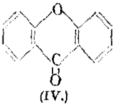
Fixation of Links.—Further information concerning the structure of xanthone is derivable from the moments found for dibromo- and for β-dinitro-xanthone. From the general order of these results the substituents are clearly in the positions 2 : 7; further (see p. 196), an independent chemical proof has been provided for the constitution of the second compound. If now we take the moment due to bromine to be 1·5 and that due to nitroxyl to be 4·0 and attribute the excess of the moment of each compound over that of xanthone to the two Br and the two NO_2 component moments in each case, it is seen that the two bromines constitute a resultant of 1·0 and the two nitro-groups one of 2·61. Application of the well-known formula for vector addition of dipole moments shows that in the two cases the individual moments lie along directions making angles with one another of 141° and 142° respectively.

In view of the possibility that the values taken above for the component moments may

be slightly too small (owing to the interactions between the 2 : 7-dipolar groups and the oxygen atom and the ketonic radical of the central ring) it is important to note the direction in which the error in the above calculation will lie. *If m be the component moments and* θ be the angle at which they act, then we have : $\cos\theta = [(\text{Resultant})^2 - 2m^2]/2m^2$. From the order of the figures above, $\cos\theta$ is negative ; obviously therefore any *increase* on the value of m will cause θ to approach the limiting value, *viz.*, 180°. Thus our calculation of the amount of widening of the 2 : 7-valency angles is a minimum estimate, and our explanation would be strengthened rather than weakened by the adoption of the more correct values, if they were obtainable, for μ_{Br} and μ_{NO_2} in these compounds.

An estimate of the degree of induction by the nitro-group on the ethereal oxygen is easily made. The distance from the centre of the oxygen atom to the point of contact of the nitrogen and carbon atoms in either the 2 or the 7 position is *ca.* 5 A. The polarisability of an ethereal oxygen atom is $0{\cdot}07 \times 10^{-23}$ e.s.u., and if the moment of the inducing dipole is taken as 4 (*i.e.*, the value for nitrobenzene), μ_{induced} becomes $2\alpha\mu . 10^{-17}/r^3 = 0{\cdot}04 \times 10^{-18}$. Such an increase scarcely affects the value of $\cos\theta$. Since, however, Sutton and Hampson (*Trans. Faraday Soc.*, 1935, **31**, 945) find that in 4-nitrodiphenyl ether considerably greater interaction moments may be operative, we will observe that if, in the case of 2:7-dinitroxanthone above, the nitro-component moment were 4·5, $\cos\theta$ would be $-$ 0·8318, and θ only 147°.

Our present results are in agreement with (IV), in which the two C–X bonds would most probably be inclined at an angle of the order 140°. The cause which could underlie the development of such a structure has been discussed by Mills and Nixon (J., 1930, 2510) : for geometrical reasons the angles between the double bond and each of the single links in $C_1{=}C_2{<}^{A}_{B}$ will be *ca.* 125° if the angle $A{-}C_2{-}B$ has the normal tetrahedral value, *viz.*, 110°. Therefore in a stabilised Kekulé benzene structure there will be an alternation of angles between successive pairs of the external C–H valencies. But since the hexagonal angle in aromatic compounds is 120°, the angle $C_1{-}C_2{-}B$ of the above unit must, in the construction of the benzene nucleus, become reduced by 5°. Thus the two external angles will together make 240°. This is all that can definitely be said regarding their values. A reasonable guess is that the strain is divided more or less equally, giving angles of *ca.* 127½° and 112½°. Our results correspond to 130° and 110°. They are therefore in accord with the theoretical prediction of Mills and Nixon (*loc. cit.*) that fusion of a benzene ring with a 6-membered ring tends towards the stabilisation in the former of that Kekulé individual which has a double bond *between* the points of attachment of the side nucleus. To a small extent the observed splaying of the 2 : 7-valency directions may be caused by the differences between the radii of the ethereal oxygen and the ketonic carbon atom in the γ-pyrone nucleus; for the reasons noted above, however, this is probably very slight. We have neglected it in the discussion of α-dinitroxanthone (later), and take the view that if the side rings of xanthone were fully mobile—*e.g.*, as in benzene itself—we should have found, instead of an angle of *ca.* 140°, one of *ca.* 120°.



(IV.)

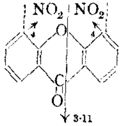
An implication of the present conclusions is that both the oxygen and the ketonic valency angles must in these substances be approximately 100°. For the former, such a result is not necessarily abnormal, since values between 90° and 180° have been reported to occur in different compounds (cf. Bernal, *Trans. Faraday Soc.*, 1934, **30**, 860 ; Bennett, *ibid.*, p. 853 ; Hampson and Sutton, *Proc. Roy. Soc.*, 1933, *A*, **140**, 562 ; Hampson, Farmer, and Sutton, *ibid.*, 1933, *A*, **143**, 158). The ketonic angle has not been so fully discussed (cf., however, LeFèvre and LeFèvre, J., 1935, 1701), but it is evidently also easily influenced by, *e.g.*, spatial requirements of attached groups. In most compounds it appears to have an angle of 110° ± 5° (Dornte, *J. Amer. Chem. Soc.*, 1933, **55**, 4126), but in some (*e.g.*, linear carbon suboxide, LeFèvre and LeFèvre, *loc. cit.*) this is presumably vanishingly small, and in others (*e.g.*, dimeric keten and tetramethyl*cyclo*butanedione, cf. J., 1935, 1751) it must approach 90°.

An implied reduction of the ketonic valency angle, therefore, does not invalidate *a priori*

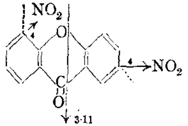
the present conclusions. Hence, dinitro- and dibromo-xanthones constitute cases additional to those recently presented by Sidgwick and Springall (J., 1936, 1532) in which physical measurements clearly show the fixation of the conjugated linkings of an aromatic ring system.

Relation of Xanthone to Diphenyl Ether and Benzophenone.—If the xanthone molecule is regarded as benzophenone and diphenyl ether superimposed, it might at first appear that the moment of xanthone should accurately equal the difference between those of the other two compounds, since in the *experimental* values for these the effects of induction are included incidentally. As stated previously, however, such a method of calculation gives a result 1·2 units too small. Three causes may be suggested for this: (1) The benzene rings in the free molecules of diphenyl ether and benzophenone are undoubtedly in a state of oscillation and rotation; in xanthone they are tied into a flat configuration—thus, since benzene is more polarisable in its plane than in other directions, induction processes will proceed farther in xanthone than in the separate molecules named. (2) The oxygen and carbonyl valency angles are probably greater in diphenyl ether and benzophenone than in xanthone; thus in the latter compound the polarisable benzo-nuclei are more behind the inducing dipoles than they are in the two separate substances; the effect of this on the induction occurs through the angle θ: the smaller θ is, the greater is $(3 \cos^2 \theta - 1)$, up to the limiting value of 2 (where $\theta = 0°$ or $180°$). Inspection of the formula used in the calculation above shows that a diminution in the angle θ corresponds to an *increase* in the induced moment. (3) The reciprocal effects between the carbonyl group and the oxygen atom should be considered. Moreover, (4) there is no certainty that in the three compounds interatomic distances are the same; since these enter the calculation as their cubes, quite slight alterations in them could materially change the magnitudes of the induced moments.

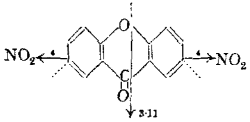
The Orientation of α-Dinitroxanthone.—Using the above results and conclusions, we have calculated the moments to be expected for each of the four possible dinitroxanthones. The values are given below their respective formulæ (V)—(VIII), the dotted lines indicating the directions the side-chain linkings would take up if the aromatic nuclei were mobile; *e.g.*, in (V) they are parallel and in (VI), (VII), and (VIII) at 120°. It is noteworthy that the change of dipole moment consequent upon the degree of valency deflection indicated by our results above—about 10°—is easily measurable. Thus if in (VII) no fixation of links were to occur, then its resultant molecular moment should be *ca.* 7. The difference between this figure and that actually found (7 − 5·8 = 1·2) corresponds to a polarisation of some 30 c.c.



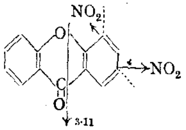
(V.) $\mu = 4·78$.



(VI.) $\mu = 4·49$.



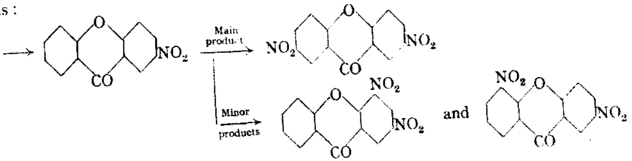
(VII.) $\mu = 5·84$.



(VIII.) $\mu = 3·11$.

The observed moment of α-dinitroxanthone is 2·98. It would therefore appear to be the 2 : 4-compound. A substance of this structure has been synthesised from 2 : 4-dinitro-2′-carboxydiphenyl ether (Ullmann, *Annalen*, **1909**, **366**, 87), but it has a higher m. p. (206°), although in appearance, solubility, etc., it shows a strong resemblance to α-dinitroxanthone, m. p. 190°. The latter preparation, upon further examination, behaved as a difficultly separable mixture. Recrystallisation from chloroform or benzene gradually raised the m. p.

from *ca.* 190° to *ca.* 198°, but even then the substance, although analytically pure and conforming to the descriptions given in the literature, had not the well-defined crystalline appearance usually associated with chemical homogeneity. The progress of the purification was followed by carrying out density and dielectric-constant measurements on benzene solutions of each batch. The polarisations (and therefore the apparent moments of the "α-dinitroxanthone") decreased with increase of m. p. down to the value now recorded for the α-dinitro-compound. The impurity being removed was therefore of higher polarity, probably either (VI) or (VII); according to this view the nitration of xanthone proceeds thus:

(I) →


Experimental.

Preparation of Substances.—Xanthone is not readily attacked by nitric acid or the halogens. Perkin (*loc. cit.*) and Richter (*loc. cit.*) dissolved the substance in mixed acids and left the solution for several hours; the chief product was then the β-dinitro-derivative, which after purification had reported m. p.'s from 260° to 262°. From the mother-liquors obtained in the crystallisation, the α-compound was isolated first by Richter, who gave the m. p. as 145—150°, but later, Graebe (*loc. cit.*) found 190°. According to the latter, xanthone and cold fuming nitric acid when left together for several days yield only the α-dinitro-derivative, apart from unchanged xanthone.

In the present work a number of unsuccessful attempts were made to mononitrate xanthone. The methods applied (potassium nitrate and sulphuric acid; nitric and acetic acids) led to the isolation of impure dinitroxanthones mixed with unattacked material. The preparations of β-dibromo- and β-dinitro-xanthone were carried out according to the directions of Dhar (J., 1916, **109**, 747). The dibromo-compound was recrystallised from absolute alcohol and had m. p. 212—213° (Found: C, 44·0; H, 1·8. Calc.: C, 44·1; H, 1·7%); β-dinitroxanthone, crystallised from chloroform, had m. p. 261—262° (Found: C, 54·6; H, 2·2. Calc.: C, 54·5; H, 2·1%).

α-Dinitroxanthone.—Xanthone (5 g.) was added to nitric acid (*d* 1·5; 50 c.c.) at 0°, and the solution left at room temperature for 4 days. Dilution, filtration, thorough washing with boiling water, and drying at 100° then afforded a white powder (*ca.* 7 g.) which softened at about 180° and was liquid by 187° (Found: C, 55·0; H, 2·3%). Admixture with β-dinitro- or 2:4-dinitro-xanthones was without ascertainable effect on this m. p.

This crude material, examined in benzene solution, showed an apparent polarisation of the order 350 c.c., corresponding to a moment of 3—4 units. Repeated recrystallisation from much chloroform finally produced a small quantity of yellow crystalline material, m. p. 196—198°, which also showed an indefinite mixed m.p. behaviour (Found: C, 54·3; H, 2·3%). The measurements recorded in detail were made on this sample.

Observations.—In the accompanying tables the symbols have the following significances: f_1, the molar fraction of the solute in each solution; *d*, the density of the solution compared with

$f_1 \times 10^6$.	ε.	*d*.	P_{12}.	P_1.
		Benzene.		
0	2·2725	0·87380	26·5863	—
		Xanthone.		
447·64	2·2790	0·87410	26·6905	259·4
800·11	2·2836	0·87433	26·7649	249·8
933·26	2·2851	0·87441	26·7897	244·5
1121·5	2·2877	0·87453	26·8316	245·3
		β-Dibromoxanthone.		
401·15	2·2832	0·87462	26·7558	449·2
1259·05	2·3036	0·87650	27·0760	415·6
2001·1	2·3211	0·87814	27·3486	407·7
2615·5	2·3351	0·87948	27·5667	401·4

$f_1 \times 10^6$.	ε.	*d*.	P_{12}.	P_1.
		α-Dinitroxanthone.		
94·20	2·2738	0·87394	26·6078	254·8
117·51	2·2741	0·87398	26·6126	250·2
237·18	2·2758	0·87416	26·6406	255·5
279·95	2·2763	0·87423	26·6488	249·7
		β-Dinitroxanthone.		
100·85	2·2772	0·87391	26·6590	747·6
111·60	2·2777	0·87392	26·6668	748·2
178·22	2·2808	0·87399	26·7147	746·8
225·55	2·2829	0·87404	26·7472	740·0

water at 4°; ε, the dielectric constant of the solution at approx. 1200 kc.; P_{12} and P_1, the apparent polarisations of the solution and the solute at the stated concentrations; α and β, the coefficients of change of dielectric constant and density with reference to f_1. The solvent used was benzene throughout, and all measurements were made at 25°.

From the above data, the polarisation at infinite dilution (${}_\infty P_1$ in following table) of each of the four solutes has been calculated by the expression ${}_\infty P_1 = A(M_1 - B\beta) + C\alpha$ (cf. J. 1936, 491). For the present solvent the constants A, B, and C are respectively 0·34085, 89·265, and 14·670.

	Xanthone.	β-Dibromoxanthone.	α-Dinitroxanthone.	β-Dinitroxanthone.
Mean α	14·36	24·90	13·76	46·50
Mean β	0·6593	2·132	1·512	1·068
${}_\infty P_1$	257·4	421·1	253·3	747·1

SUMMARY.

The dipole moment of xanthone is found to be 3·11. The excess of this value over that calculated from diphenyl ether (*ca.* 1·0) and benzophenone (*ca.* 3·0) is largely due to electrostatic induction effects operating between different groups in the molecule. The amount of such induction is calculated. A fully dipolar form (μ = *ca.* 21) cannot make more than a 3% contribution to the real structure.

The observed moments of two 2 : 7-disubstituted xanthones show that the links holding the substituents in each case are at 141—142° to each other, *i.e.*, that a nearly complete fixation of double and single bonds occurs in the xanthone skeleton. This result is in agreement with the theory of Mills and Nixon. On this basis the moments of the four possible dinitroxanthones have been calculated. "α-Dinitroxanthone" is thereby seen to be a slightly impure specimen of 2 : 4-dinitroxanthone.

UNIVERSITY COLLEGE (UNIVERSITY OF LONDON). [*Received, June 20th,* 1936.]

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35. *The Structure of Some Derivatives of Fluorene and Fluorenone.*

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No undisputed space formula for fluorene and its derivatives has yet been assigned. Mills, Palmer, and Tomkinson (J., 1924, **125**, 2365) were of the opinion that a strainless configuration for the fluorene molecule could be achieved by the planes of the benzene rings becoming inclined to the 5-ring. The stereochemical implications of such a non-planar structure have been widely investigated, with somewhat equivocal results, reviewed by Cook and Iball (*Chem. and Ind.*, 1936, **55**, 467). From their summary it is obvious that the authenticity of allegedly geometrically isomeric 9-substituted fluorenes is highly doubtful, and that no unquestioned resolution of an unsymmetrically substituted fluorene into optical isomers has yet been made.

Some physical data are on record having a bearing on the present question. Hengstenberg and Mark (*Z. Krist.*, 1929, **70**, 289) and Cook and Iball (*loc. cit.*) examined crystalline fluorene by means of *X*-rays. The observations are apparently not identical. The latter authors, however, state that they can reconcile their results with a space formula for the molecule in which the aromatic nuclei are flat regular hexagons inclined at 20° about the common links to the plane of the pentagonal ring to which they are attached.

This paper records certain dipole-moment determinations (Table I) and contains a discussion of their significance in relation to the general problem.

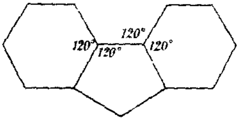
Possible Spatial Configurations.—In attempting to consider the above results, it at once becomes obvious that in default of definite experimental evidence certain assumptions have to be made. We will, therefore, begin by supposing the five-membered ring to be regular, *i.e.*, with all its angles 108°, and since 120° is the internal angle of each aromatic ring, it follows that (*if the molecule remains planar*) the aromatic rings are distorted by 12° from a diphenyl-containing structure (I), thus presenting form (II). It is noteworthy that structure (I) is not only unlikely in view of the strain imposed on the 5-membered

TABLE I.

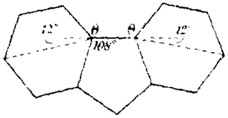
Substance.	P_T.	$[R_L]_D$.	μ, found.
Fluorene	70	56	0·82
* 2 : 7-Dinitrofluorene	137	78	*ca.* 1·7
2 : 5- ,,	1100	68	7·06
2 : 7-Dibromofluorene	73	72	0·22
Fluorenone	289	57	3·35
2-Nitrofluorenone	816	63	6·04
2 : 7-Dinitrofluorenone	547	70	4·80
* 2 : 5- ,,	830	70	*ca.* 6
2 : 7-Dibromofluorenone	481	73	4·44

* Owing to the limited solubility of these substances (maximum f_1 *ca.* 0·0002), the $_\infty P_T$ should be regarded as being only an approximation.

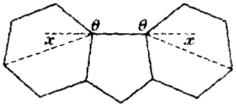
-ing but is definitely excluded by our experimental results (*e.g.*, the non-identity of the moments of fluorenone and its 2 : 7-disubstituted derivatives).



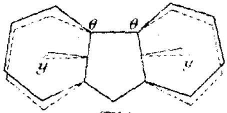
(I.)



(II.)



(IIa.)



(IIb.)

Formula (II), however, requires that the external angle, θ, common to the 5- and each 6-membered ring, must be 132°. *A priori* little is known regarding the possibility of this, but we note that the natural external angles for regular pentagons and hexagons are 126° and 120° respectively. One might, therefore, expect the external angle to become *ca.* 123° by a *cis*- or *trans*-rotation (illustrated in II*b*) of the six-membered rings through *ca.* 30° around the links common to them and the 5-membered ring. Adopting this configuration, we have calculated (cf. Table II) the dipole moments of the substances examined, taking the moments of the $-NO_2$ and $-Br$ groups as 4·17 and 1·64 respectively. These are the moments found for 4-nitrodiphenyl and 4-bromodiphenyl (Le Fèvre and Le Fèvre, J., 1936, 1130); in assuming these values we dispense with the necessity of calculating in each case the moments induced in the polarisable nuclei by the principal moment. This we feel justified in doing since fluorene and diphenyl are not greatly dissimilar in their molecular form and polarisability.* The values of the moments due to the $\cdot CH_2\cdot$ group in fluorene and the $\rangle C{=}O$ group in fluorenone, used in these calculations, were obtained by direct measurement on the two substances.

It will be observed that for neither the *trans*- nor the *cis*-form is there good agreement. However, it might be urged that a deflection of the order 30° must be regarded as an upper limit, because if this value be increased the common external angle θ will become too small (*i.e.*, less than 123°) and a redevelopment of strain will occur in it. Since a non-planar molecule of this type, however, already contains strain due to the distortion of two of the external carbon valency directions of each benzene ring from their normal plane, a tendency towards a strainless form may exist in which the deflection is intermediate between 0° and 30°. The remainder of the calculations in Table II were accordingly made; the value of μ, found, is added in parentheses after the name of each substance.

* Cf. footnote on p. 206.

TABLE II.

Deflection.	μ, calc. trans.	μ, calc. cis.	Deflection.	μ, calc. trans.	μ, calc. cis.	Deflection.	μ, calc. trans.	μ, calc. cis.	Deflection.	μ, calc. trans.	μ, calc. cis.
2 : 7-Dinitrofluorene (1·7 *).			2 : 7-Dibromofluorene (0·2).			2-Nitrofluorenone (6·0).			2 : 5-Dinitrofluorenone (6 *).		
0°	0·9	0·9	0°	0·1	0·1	0°	5·9	5·9	0°	5·4	5·4
10	0·9	1·6	10	0·1	0·5	10	5·9	5·9	10	5·4	5·4
20	1·1	2·7	20	0·1	1·0	20	5·9	5·9	20	5·3	5·3
30	1·2	3·8	30	0·0	1·4	30	6·0	6·0	30	5·3	5·3
2 : 7-Dinitrofluorenone (4·8).			2 : 7-Dibromofluorenone (4·4).			2 : 5-Dinitrofluorene (7·1).					
0	5·1	5·1	0	4·0	4·0	0	6·7	6·7			
10	5·1	5·2	10	4·0	4·1	10	6·6	6·6			
20	5·2	5·8	20	4·1	4·2	20	6·6	6·6			
30	5·4	6·5	30	4·2	4·4	30	6·5	6·5			

* Cf. Table I.

It is seen that no *one* form adopting a deflection value between + 30° and − 30° (*trans*- and *cis*-extremes) can be considered as suggesting a spatial structure typical of the series.

We have already written a brief note (*Chem. and Ind.*, 1935, **55**, 545) in which it was pointed out that the dipole moment we obtain in *benzene solution* for 2 : 7-dinitrofluorenone is considerably smaller than that calculated on a basis of Cook and Iball's structure, that is, our 20° *cis*-deflection. We appreciate that Cook and Iball advance their non-planar configuration for *solid fluorene*, and that this non-agreement need not indicate more than that a non-planar molecule of the type they describe cannot exist in solution. Essentially the same comment has been made by Cook and Iball (*loc. cit.*) on the incompatibility of the extant stereochemical evidence and their suggested structure.

The effect of the variation of one of the basic assumptions made above should now be mentioned: if in the transition of (I) into (II) an angle (x in II*a*) *less* than 12° were involved (*i.e.*, if the hypothesis of a regular pentagon were abandoned) the strain on the external angle would be less and the consequent departure of the molecule from one plane (y in II*b*) need not be so great. The corresponding calculated results are in Table III.

TABLE III.

Substance.	μ, calc. *trans*-Config.	μ, calc. *cis*-Config.	μ, calc. *trans*-Config.	μ, calc. *cis*-Config.	μ, calc. *trans*-Config.	μ, calc. *cis*-Config.
	$x = 4°$; $y = 0°$.		$x = 4°$; $y = 10°$.		$x = 4°$; $y = 20°$.	
2 : 7-Dinitrofluorene	0·2	0·2	0·2	1·3	0·0	2·5
2 : 7-Dinitrofluorenone	3·9	3·9	4·0	4·1	4·1	4·8
2 : 7-Dibromofluorene	0·6	0·6	0·6	0·8	0·5	1·1
2 : 7-Dibromofluorenone	3·6	3·6	3·6	3·8	3·7	3·8
2-Nitrofluorenone	5·5	5·5	5·5	5·5	5·6	5·6
2 : 5-Dinitrofluorene	7·4	7·4	7·3	7·3	7·3	7·3
2 : 5-Dinitrofluorenone	6·0	6·0	6·0	6·0	5·9	5·9
	$x = 8°$; $y = 0°$.		$x = 8°$; $y = 10°$.		$x = 8°$; $y = 20°$.	
2 : 7-Dinitrofluorene	0·3	0·3	0·4	1·3	0·5	2·5
2 : 7-Dinitrofluorenone	4·5	4·5	4·5	4·7	4·7	5·3
2 : 7-Dibromofluorene	0·4	0·4	0·4	0·6	0·3	1·0
2 : 7-Dibromofluorenone	3·8	3·8	3·8	3·8	3·9	4·0
2-Nitrofluorenone	5·7	5·7	5·7	5·7	5·8	5·8
2 : 5-Dinitrofluorene	7·0	7·0	7·0	7·0	6·9	6·9
2 : 5-Dinitrofluorenone	5·7	5·7	5·7	5·7	5·6	5·6

It can be seen that here again no general solution emerges for any one form although the experimental figures seem to fit less badly the configurations with $x = 8°$ and $y = 10$—20°. We note that for the latter value ($y = 20°$) the external angle is practically strainless ($\theta = 124°$), and that the results would not be in great disagreement with the existence of these molecules in solution as a mixture of *cis*- and *trans*-strainless forms.

Finally, we have considered the possibility that each derivative has a different struc-

ture, intermediate between two extreme forms in which the benzene rings are not regular hexagons but have some less symmetrical form. On this hypothesis the 2 : 4 : 5 : 7-C–H valency directions will differ by $\pm \phi°$ respectively from those which they would otherwise have in a symmetrical molecule. We will illustrate the applicability of the proposal to the flat structure specified under (II) above. We find that if $\phi = 7\frac{1}{2}°$ the experimental results can just be included in the range of the calculated figures (cf. Table IV).

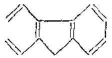
TABLE IV.

Substance.	μ, calc., for $\phi = +7\frac{1}{2}°$.	μ, found.	μ, calc., for $\phi = -7\frac{1}{2}°$.
Fluorene	—	0·82	—
* 2 : 7-Dinitrofluorene	0·17 ↑	*ca.* 1·7	1·96 ↓
2 : 5- „	7·31	7·06	5·87
2 : 7-Dibromofluorene	0·56 ↑	0·22	0·28 ↓
Fluorenone	—	3·35	—
2-Nitrofluorenone	5·55	6·04	6·16
2 : 7-Dinitrofluorenone	4·00	4·80	6·13
* 2 : 5- „	5·95	*ca.* 6	4·73
2 : 7-Dibromofluorenone	3·61	4·44	4·45

* Cf. footnote to Table I.

(*In certain cases for the purpose of comparison attention has to be paid to the direction in which the* calculated resultant moment lies. This is indicated by arrows. The direction of the μ_{C-H} is taken as ↑ and the $\mu_{C=O}$ as ↓.)

This value for ϕ coincides with one which can be forecast from an application to formulæ (III*a*) and (III*b*) of the argument which Mills and Nixon (J., 1930, 2510) have used fruitfully in the cases of 5-hydroxyhydrindene and *ar*-tetrahydro-β-naphthol, namely, that the

(III*a*.)  (III*b*.)

C–H valency directions in such molecules will make, alternately, greater and smaller angles with their adjacent C–C bonds. The magnitudes of these angles are uncertain; for a six-membered ring they should result from the distribution of 5° of strain over two angles of 125° and 110° each; $127\frac{1}{2}°$ and $112\frac{1}{2}°$ thus seem a fair choice; ϕ in (III*a*) and (III*b*) therefore becomes $\pm 7\frac{1}{2}°$.

General Conclusions.—(1) Although our results do not point to one specific configuration, certain structures are definitely inapplicable. (2) The hypotheses that these compounds exist in solution as a mixture of non-planar forms of the type $x = 8°$, $y = 20°$ considered above, or that they are flat degenerate forms between the extremes (III*a*) and (III*b*), are not excluded.

The Dipole Moments of Fluorene and Fluorenone.—The moments observed for these compounds are unexpectedly high when considered in the light of those of diphenylmethane ($\mu = 0·23$; Hampson, Farmer, and Sutton, *Proc. Roy. Soc.*, 1933, **143**, 147) and benzophenone ($\mu = 2·99$; Müller, *Physikal. Z.*, 1933, **34**, 689) respectively. An important contrast between fluorene and diphenylmethane is, however, the much greater reactivity of the hydrogen atoms of the methylene group in the former hydrocarbon; compare the formation of sodium and potassium derivatives by melting with the corresponding alkali hydroxides (Weissgerber, *Ber.*, 1901, **34**, 1659; 1908, **41**, 2914). In this respect it resembles indene (Weissgerber, *Ber.*, 1909, **42**, 572) and the parent compound *cyclo*pentadiene (Thiele, *Ber.*, 1901, **34**, 68). An explanation of this reactivity has been advanced by Goss and Ingold (J., 1928, 1268) depending on the fact that in the *cyclo*pentadiene ring the electrons requisite for the stabilising sextet (supplied by the three olefinic bonds in benzene) can only be provided by the partial appropriation of the bonding electrons of one of the methylene hydrogen atoms. This hydrocarbon and its derivatives therefore have properties analogous to those of an acid in so far as one of their hydrogen atoms is predisposed to leave the molecule as a proton. It is therefore not incompatible with this to find that in fluorene the H⟶C dipoles evidently have a value several times greater than they possess in an ordinary methylene group.

Between fluorene and fluorenone, on the one hand, and diphenylmethane and benzophenone, on the other, there exists the further difference that in the former compounds the benzene rings are fixed close to the same plane as the 9-carbon atom, whilst in the latter pair the rings are free to undergo rotation, etc.,* about the links by which they are attached to the central carbon atom. The consequence of this is that in both fluorene and fluorenone, since the chief moment of the molecule in both cases operates through the 9-position and *in the plane to which reference has just been made, circumstances are so arranged that the* induction of subsidiary moments in the polarisable benzo-nuclei can occur almost to the maximum extent possible.

The magnitudes of these induced moments can be calculated if the value of the chief moment, the polarisability of the structure in which the induction occurs, the distances between the mass centre of the latter and the point of operation of the inducing dipole, the dielectric constant of the intervening medium, etc., are known.

In the case of fluorenone the chief moment is the bond moment appropriate to the ketonic linkage, *viz.*, 2·5 (Sidgwick, " The Covalent Link in Chemistry," 1933, **153**). Thus on the basis of a flat model in which two regular hexagons of side 1·42 A. are fused to a regular pentagon of the same side length, in which the polarisability of the benzene rings is that found by Stuart and Volkmann (*Ann. Physik*, 1933, **18**, 121) for the benzene molecule in its plane, we have : †

moment induced at mass centre of attached nuclei in direction parallel to the direction of the ketonic link

$$= \frac{\text{polarisability} \times \text{inducing moment}}{(\text{distance})^3} (3 \cos^2 \beta - 1) \frac{(\varepsilon + 2)}{3\varepsilon}$$

where β = angle between line joining mass centre to seat of dipole and direction of dipole. Calculation shows that

$$\beta = 38{\cdot}9°, \text{ distance} = 3{\cdot}34 \text{ A.};$$

hence if ε is taken as 2·3,

$$\mu \text{ induced} = 0{\cdot}42 \text{ unit}$$

Therefore, molecular resultant = 2·5 + 2 × 0·42 = 3·34 units.

This is in excellent agreement with the value, 3·35, found experimentally. A similar calculation cannot be carried out in the case of fluorene owing to the uncertainty of the value to be taken for the moment of the methylene group in view of the abnormal chemical behaviour of this radical.

Previous Measurements.—Four of the present compounds had been studied by Bergmann, Engel, and Hofmann (*Z. physikal. Chem.*, 1932, *B*, **17**, 92), and their results are tabulated beside ours :

Substance.	B., E., & H. $[R_L]_D$.	B., E., & H. μ.	Present authors. $[R_L]_D$.	Present authors. μ.
Fluorene	60	0·28 ~ 0	56	0·82
2 : 7-Dibromofluorene	75	0	72	0·22
Fluorenone	63	3·29	57	3·35
2-Nitrofluorenone	94	5·44	63	6·04

In our work, because of the limited solubility of most of the substances, refractivities were not directly measured; instead, they were calculated from the experimental values

* In the cases of the diphenyl compounds mentioned on p. 203, it will be realised that free rotation of the remote phenyl group will not affect either the magnitudes or the directions of the moments induced therein, because both induced and inducing moments lie along the same axis. The situation is different with the fluorene derivatives: here the inducing and resultant moments induced in the side rings lie along directions which are neither collinear nor parallel. Because of the anisotropy of polarisability of the benzene rings, therefore, the induced moments will vary with the process of tilting the 6-rings out of the plane of the central 5-ring.

† We consider the polarisability of a benzene ring as situated at its centre. A more detailed calculation might be made in which the CH groups are taken separately. We have recently made calculations on both bases for the somewhat similar case of xanthone. (See preceding paper.)

for fluorene (56) and fluorenone (57)—which can be obtained with a reasonable degree of accuracy—by subtraction of the refractive equivalents for the necessary number of hydrogen atoms, and addition of the appropriate atomic refractions for the substituent groups.

EXPERIMENTAL.

Preparation of Materials.—Fluorene was recrystallised from alcohol immediately before use, m. p. 114—115°. 2 : 7- and 2 : 5-Dinitrofluorenes were prepared as described by Courtot (*Ann. Chim.*, 1930, **14**, 5; compare Anantakrishnan and Hughes, J., 1935, 1607).

2 : 7-Dibromofluorene also was obtained by Courtot's method (*loc. cit.*) but was repeatedly recrystallised from ethyl acetate instead of carbon disulphide; m. p. 165° (Courtot gives 162—163°). The ketones were prepared in each instance by the oxidation of the purified corresponding fluorene derivative. They were finally recrystallised from acetic acid; their m. p.'s agreed with those recorded in the literature.

Measurements.—In the following tables, the symbols have their usual significance, ε being measured at approximately 1200 kc.; the temperature of measurement was 25° throughout, and the solvent, benzene.

f_1.	$\epsilon_{25°}$.	$d_{4°}^{25°}$.	$P_1f_1 + P_2f_2$.	P_1.
		Benzene.		
0	2·2725	0·87380	26·5863	—
		Fluorene.		
0·000488	2·2733	0·87398	26·6072	69·53
0·001706	2·2750	0·87444	26·6547	66·71
0·002714	2·2763	0·87484	26·6918	65·47
0·003550	2·2771	0·87515	26·7192	64·02
		2 : 7-*Dinitrofluorene.*		
0·000199	2·2736	0·87401	26·6082	136·2
0·000277	2·2740	0·87409	26·6164	134·7
0·000278	2·2741	0·87409	26·6178	139·8
		2 : 5-*Dinitrofluorene.*		
0·000107	2·2800	0·87394	26·6984	1072·7
0·000203	2·2848	0·87407	26·7703	932·7
0·000310	2·2897	0·87422	26·8437	856·9
0·000489	2·2969	0·87446	26·9520	773·9
		2 : 7-*Dibromofluorene.*		
0·001179	2·2739	0·87596	26·6399	72·04
0·001299	2·2741	0·87618	26·6462	72·67
0·001998	2·2750	0·87749	26·6781	72·49
0·003017	2·2761	0·87934	26·7231	71·92

f_1.	$\epsilon_{25°}$.	$d_{4°}^{25°}$.	$P_1f_1 + P_2f_2$.	P_1.
		Fluorenone.		
0·000902	2·2874	0·87428	26·8210	286·84
0·002414	2·3120	0·87513	27·2048	282·83
0·002999	2·3214	0·87545	27·3510	281·51
0·004199	2·3411	0·87607	27·6564	281·38
		2-*Nitrofluorenone.*		
0·000131	2·2793	0·87391	26·6892	815·30
0·000170	2·2813	0·87394	26·7194	807·75
0·000326	2·2896	0·87412	26·8428	814·67
0·000554	2·3014	0·87434	27·0189	807·36
		2 : 7-*Dinitrofluorenone.*		
0·000081	2·2752	0·87390	26·6281	543·21
0·000116	2·2764	0·87396	26·6462	541·70
0·000400	2·2858	0·87433	26·7910	538·38
0·000561	2·2911	0·87454	26·8723	536·01
		2 : 5-*Dinitrofluorenone.*		
0·000113	2·2775	0·87390	26·6640	712·39
0·000152	2·2785	0·87393	26·6802	644·12
0·000197	2·2791	0·87397	26·6907	555·83
0·000232	2·2795	0·87400	26·6980	508·18
		2 : 7-*Dibromofluorenone.*		
0·000067	2·2744	0·87392	26·6165	476·9
0·000143	2·2764	0·87407	26·6484	459·7
0·000334	2·2809	0·87443	26·7198	425·7
0·000545	2·2845	0·87489	26·7771	376·6

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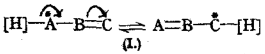
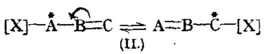
36. *Retention of Asymmetry and Inversion of Configuration during Anionotropic Change. The Conversion of* (−)α-*Phenyl*-γ-*methylallyl Alcohol into* (+)γ-*Phenyl*-α-*methylallyl Alcohol.*

By J. KENYON, S. M. PARTRIDGE, and H. PHILLIPS.

IN 1933 Ingold and Wilson (J., 1493) began a series of investigations to ascertain whether asymmetry is retained during prototropic (I) and anionotropic (II) changes in which a proton



(I.)



(II.)

(I) or an anion (II) moves from one asymmetric centre to a new asymmetric centre arising as a result of the isomeric change. After a detailed discussion of the problem, and exploratory experiments with both prototropic and anionotropic systems (*loc. cit.*), the mutually interconvertible azomethines (III) and (IV)

$$\text{(III.)}\quad \begin{matrix}\text{Me}\\\text{Ph}\end{matrix}\!>\!\text{C[H]}\cdot\text{N:C}\!<\!\begin{matrix}\text{Ph}\\\text{C}_6\text{H}_4\text{Cl }(p)\end{matrix} \;\rightleftharpoons\; \begin{matrix}\text{Me}\\\text{Ph}\end{matrix}\!>\!\text{C:N}\cdot\text{C[H]}\!<\!\begin{matrix}\text{Ph}\\\text{C}_6\text{H}_4\text{Cl }(p)\end{matrix}\quad \text{(IV.)}$$

were selected for study, and from the equilibrium mixture obtained after the isomerisation of the optically active isomeride (III), the isomeride (IV) was isolated in an optically inactive condition. Later, kinetic studies of the rates of racemisation and of tautomeric change led Hsü, Ingold, and Wilson (J., 1935, 1778) to conclude that the racemisation observed during the prototropic change of azomethines did not occur during the ionisation which precedes the tautomeric change, and therefore that mesomeric anions were capable of retaining their optical activity. Additional evidence in support of this conclusion was drawn from the influence of constitutional factors on the rates of racemisation of prototropic compounds (Wilson, J., 1934, 98) and from comparisons of the rates of racemisation and bromination of optically active ketones (Ingold and Wilson, J., 1934, 773; Hsü and Wilson, J., 1936, 623).

Contemporaneously with the above investigations, we have studied the anionotropic system (V) $\rightleftharpoons$ (VI), mainly in order to throw light on the nature of the isomerism undergone by the more symmetrically substituted (+)$\alpha\gamma$-dimethylallyl alcohol (Hills, Kenyon, and

$$\text{(V.)}\quad (-)\text{Ph}\cdot\text{CH[OH]}\cdot\text{CH=CHMe} \qquad\qquad (+)\text{Ph}\cdot\text{CH=CH}\cdot\text{CH[OH]Me}\quad\text{(VI.)}$$

Phillips, *Chem. and Ind.*, 1933, **52**, 660; J., 1936, 580). We have been able to obtain evidence that when (V) is converted into (VI), asymmetry is maintained, and that the new asymmetric centre produced has the opposite configuration to that of the original asymmetric centre.

Conversion of (—)*α-Phenyl-γ-methylallyl Alcohol into* (+)*γ-Phenyl-α-methylallyl Alcohol.*—The preparation of the (+) and the (—) alcohol (VI) has already been described (Kenyon, Partridge, and Phillips, J., 1936, 85); the (+) and the (—) alcohol (V) have now been prepared by the recrystallisation of the quinidine salt of dl-*α-phenyl-γ-methylallyl hydrogen phthalate* first from methyl acetate and secondly from acetone. The rotatory powers of the quinidine salts and the hydrogen phthalic esters are in Table I. The (—)α-phenyl-γ-methylallyl alcohol (see Table II) obtained by saponification of its hydrogen phthalic ester with alcoholic soda gave on reduction (+)phenyl-*n*-propylcarbinol with a rotatory power closely agreeing with that obtained by the direct resolution of *dl*-phenyl-*n*-propylcarbinyl hydrogen phthalate (Kenyon and Partridge, J., 1936, 128). It is therefore probable that both the saturated and the unsaturated alcohol have been obtained optically pure. The rotatory power of (—)α-phenyl-γ-methylallyl alcohol remained unchanged during 15 weeks at room temperature.* It is also stable to alkalis, since it was not converted into its isomeride to any appreciable extent when it was (*a*) left in contact with 20 vols. of 0·1*N*-sodium hydroxide for 14 days, (*b*) boiled under reflux with aqueous sodium hydroxide, or (*c*) heated with anhydrous potassium carbonate at 100° for 2 hrs. In acid solution it changes fairly rapidly: a solution of the (—)alcohol, with $\alpha_{5461}^{20°}$ —14·98° (*l*, 0·25), in 0·5% aqueous acetic acid after standing at room temperature for 40 hrs. gave (+)γ-phenyl-α-methylallyl alcohol with $\alpha_{5461}^{20°}$ + 0·69° (*l*, 0·5). Considerable racemisation occurred, therefore, since (+)γ-phenyl-α-methylallyl alcohol of the same degree of optical purity as that of the (—)alcohol used would have approximately $\alpha_{5461}^{20°}$ + 21·0° (*l*, 0·5).

Conversion of Derivatives of (—)*α-Phenyl-γ-methylallyl alcohol into the Corresponding Derivatives of* (+)*γ-Phenyl-α-methylallyl Alcohol.*—In agreement with Burton's conclusions (J., 1928, 1650; 1929, 455) that the anionic stability of the migratory groups X (*i.e.*, the strengths of the acids HX) partly determines the ease of conversion, the esters of (—)α-phenyl-γ-methylallyl alcohol isomerised more readily than did the parent alcohol. Even at ordinary temperatures and under diminished pressure (—)α-phenyl-γ-methylallyl hydrogen phthalate

* (Added in proof) After 18 months the rotatory power had fallen to $\alpha_{5461}^{20°}$ — 15·1° (*l*, 0·25).

TABLE I.

	Solvent.	c.	$[\alpha]_{5893}$.	$[\alpha]_{5790}$.	$[\alpha]_{5461}$.	$[\alpha]_{4359}$.
Quinidine salt of (−)α-phenyl-γ-methylallyl hydrogen phthalate	$CHCl_3$	4·64	+122·7°	+126·0°	+147·5°	+266°
Quinidine salt of (+)α-phenyl-γ-methylallyl hydrogen phthalate	$CHCl_3$	3·05	+131·0	+140·2	+160·2	+240
(−)α-Phenyl-γ-methylallyl hydrogen phthalate	Et_2O	5·00	− 17·1	− 20·0	− 22·4	− 47
(+) ,, ,, ,,	Et_2O	3·85	+ 15·5	+ 17·8	+ 20·0	+ 42

TABLE II.

The Observed Rotatory Powers (1, 0·5) *of* (−)*α-Phenyl-γ-methylallyl Alcohol.*

t.	α_{5790}.	α_{5461}.	α_{4359}.	t.	α_{5790}.	α_{5461}.	α_{4359}.
18·0°	−29·69°	−34·17°	—	50·0°	−22·90°	−26·55°	−47·8°
20·0	29·16	33·59	−64·0°	62·5	20·62	23·71	45·25
30·7	26·93	31·31	59·4	66·0	20·07	23·13	44·15
34·8	26·07	30·21	57·0	71·0	19·12	22·07	42·4
40·5	24·79	28·74	54·25	20·0 (after cooling)	29·15	33·69	64·0

t = 15·9°, 25·8°, 35·3°, 46·5°; $d^{t°}_{4°}$ = 1·0110, 1·0046, 0·9954, 0·9884 respectively.

slowly changed to a pasty mass which re-solidified after about 10 days. Viewed under the microscope the crystals maintained their shape, but their surfaces became covered with a viscous liquid. The liquid portions appeared to travel towards the centre of the crystal, which was finally composed of two forms of smaller crystals—fine hairs, corresponding to (+)γ-phenyl-α-methylallyl hydrogen phthalate, and rhombic crystals, corresponding to the *dl*-analogue, the whole mass retaining the essential shape of the original crystal. Similarly, when heated, the *dl*-hydrogen phthalic ester melted at 93—94°, but this was not its true m. p., for the resolidified ester was proved to contain *dl*-γ-phenyl-α-methylallyl hydrogen phthalate which can be readily detected since it forms a crystalline salt with cinchonidine (Kenyon, Partridge, and Phillips, *loc. cit.*) but not with quinidine. When mixed with *dl*-γ-phenyl-α-methylallyl hydrogen phthalate, the *dl*-α-phenyl ester melted at 92—93°. Details of other experiments in which the (−)α-phenyl ester was kept at various temperatures for different periods of time are given in Table III: it will be seen that as much as 70% of the (−)α-phenyl-γ-methylallyl hydrogen phthalate taken has been converted into its optically pure (+)γ-phenyl isomeride.

As is shown by the data given in Table IV (in which ε is the dielectric constant of the solvent), the isomerism undergone by the (−)α-phenyl ester in solution was more markedly affected by increase in temperature than by any change in the dielectric constant of the solvent, although, as in the case of the conversion of α-phenylallyl *p*-nitrobenzoate into cinnamyl *p*-nitrobenzoate (Burton, *loc. cit.*), the isomeric change was faster in solvents with high dielectric constants; *e.g.*, in benzonitrile the isomeric change was complete in 2 days, whereas in benzene 13 days were required.

Hyperbolæ were obtained when the rotatory powers of two solutions (Table V) of (−)α-phenyl-γ-methylallyl hydrogen phthalate, (i) c, 1·5 and (ii) c, 3·00 in carbon disulphide, were plotted against time. When t_n was plotted against $\log_{10}(A_0 - A_\alpha) - \log_{10}(A_n - A_\alpha)$, where t_n is time in hours, A_0 the initial rotation, A_α the final rotation, and A_n the rotation of the solution at time t_n, straight lines were obtained for each solution, and the velocity constant calculated from the slope of the lines proved to be in both cases 0·017, showing that the reaction was unimolecular.

In a similar manner the velocity constants (k) of the same reaction in benzene solution at different temperatures were calculated from the rotation data given in Table VI. The values of these constants when plotted against t_n gave a hyperbola, indicating that the rate of reaction approached infinity between 55° and 60°. When log k_T was plotted against T, the absolute temperature at which k_T was measured, a straight line was obtained with slope 2/0·0032, whence E, the energy of activation of the reaction, is 28,800 cals.

TABLE III.

Conversion of (—)α-Phenyl-γ-methylallyl Hydrogen Phthalate into (+)γ-Phenyl-α-methylallyl Hydrogen Phthalate at Different Temperatures in the Absence of Solvents.

Time.	Temp.	Rotatory power of final product in CS_2 (*l*, 2). $[\alpha]_{5790}$.	$[\alpha]_{5461}$.	$[\alpha]_{4358}$.	*c*.	% Final product optically pure.*	
11 days	18—20°	+15·5°	+19·0°	+39·5°	2·20	42·5	*a*
15 ,,	,,	—	27·4	—	2·45	61·0	
18 ,,	24—26	27·8	30·6	58·6	2·40	67·0	
19 ,,	,,	28·0	33·0	69·0	2·65	73·0	
20 ,,	,,	30·3	33·8	72·0	2·80	74·6	
21 ,,	,,	31·4	33·0	68·0	2·65	73·0	
22 ,,	,,	31·1	33·7	—	2·54	74·5	
23 ,,	,,	30·3	33·2	65·6	2·66	73·6	
11 ,,	18—20	5·5	6·6	—	1·89	14·5	i *b*
20 ,,	20	—	25·5	—	2·50	57·0	ii
10 mins.	75	17·6	21·2	40·8	2·50	47·0	i *c*
5 ,,	77	20·4	21·8	45·0	2·50	49·0	ii
3 ,,	80—82	24·4	27·4	53·3	2·50	61·5	iii
5 ,,	,,	24·6	27·6	51·0	2·50	62·0	iv
10 ,,	,,	18·0	20·0	36·8	2·50	49·0	v
5 ,,	94	10·3	10·9	22·2	4·78	24·0	vi

(*a*) Portions of one preparation of the (—)ester, m. p. 80—81°, were sealed up in tubes: determinations of rotatory power were made after the periods stated.

(*b*) (i) Kept at 11 mm. in a desiccator; (ii) kept at <0·1 mm. in a sealed tube.

(*c*) Portions of a second preparation of the (—)ester, m. p. 80—81°. (iii) From the heated material (1·0 g.) there were isolated *dl*-γ-phenyl-α-methylallyl hydrogen phthalate, m. p. 93—94° (0·344 g.), and (+)γ-phenyl-α-methylallyl hydrogen phthalate, m. p. 68—69° (0·205 g.), with $[\alpha]_{5461}$ +45·0° (*c*, 1·025; *l*, 2) in CS_2.

* Calculated on $[\alpha]_{5461}$ as being the most accurate values.

TABLE IV.

Transformation of (—)α-Phenyl-γ-methylallyl Hydrogen Phthalate into (+)γ-Phenyl-α-methylallyl Hydrogen Phthalate at Different Temperatures in Solvents.

Solvent.	Initial [α] of soltn. $[\alpha]_{5893}$.	$[\alpha]_{5461}$.	$[\alpha]_{4358}$.	*c*.	Temp.	Time.	Final [α] of soltn. $[\alpha]_{5893}$.	$[\alpha]_{5461}$.	$[\alpha]_{4358}$.	% Final product optically pure.	[α] of pure (+)γ-phenyl ester. $[\alpha]_{5893}$.	$[\alpha]_{5461}$.	$[\alpha]_{4358}$.	*c*.	ε.
C_6H_{12} [10]	—	—	—		82°	0·5 min.	—	−20·0°[1]	—	0	—	—	—		2·05
,,	—	—	—		82	3 ,,	—	+10·0[2]	—	22	—	—	—		
,,	—	—	—		82	30 ,,	—	+20·0[3]	—	44	—	—	—		
C_6H_6	−12·1°	−13·3°	−34·5°	3·06	20	13 days	+3·2°	+3·3[4]	+7·7°	30	+4·0°	+5·1°	+7·8°	5·00	2·28
CS_2	+0·3	+0·2	−0·1	2·66	46	5 hrs.	+22·0	+26·0[5]	+50·7	58	+37·4	+44·7	+87·4	5·00	2·64
Et_2O	−17·1	−22·4	−47·6	1·94	20	134 days	—	−14·0[6]	−26·7	33	−13·9	−16·3	−32·3	5·00	4·34
$CHCl_3$	—	−15·7	−34·1	5·12	20	22 hrs.	0	0[7]	0	39	+1·8	+2·2	+5·3	5·00	
C_6H_5Cl	—	+1·5	—	2·85	20	6 days	—	+9·0	+15·8	31	—	+29·2	—	3·25	
C_5H_5N	−3·8	−5·4	−12·7	4·35	95	<30 mins.	+11·0	+13·4	+25·3	30	+19·8	+24·2	+43·0	5·00	12·50
$COMe_2$	−21·5	−26·0	−54·6	3·85	20	17 days	—	−6·7	—	52	−10·3	−12·6	−22·3	5·00	21·3
EtOH	−44·3	−52·0	−109	1·50	20	5 ,,	—	−4·7	−6·7	—[8]	−13·5	−15·4	−28·0	5·00	25·70
PhCN	—	−12·1	—	4·00	20	2 ,,	—	+5·9	—	27	—	+21·6	—	2·75	26·5
MeOH	−25·1	−33·0	−65·3	4·04	20	67 hrs.	—	−2·0	—	—[9]	−7·2	−8·4	−15·3	14·60	33·7
$CH_3·CO_2Et$	−26·7	−34·0	−64·0	3·10	20	48 days	—	−9·7	−17·0	41	−19·0	−23·7	−41·5	5·00	6·4
Dioxan	−9·3	−12·7	−22·6	5·13	20	13 ,,	−9·3	−12·7	−22·6	0	−7·2	−9·2	−17·7	5·20	?
,,	,,	,,	,,	,,	95	10 mins.	—	+15·6	—	35[11]	—	—	—	—	

Ester recovered and rotatory power determined, [1] in ether (*c*, 1·14); [2, 3] in CS_2 (*c*, 2·50); [4] gave $[\alpha]_{5461}$ +13·6° in CS_2; [5, 7] gave $[\alpha]_{5461}$ +17·0° in CS_2; [11] gave $[\alpha]_{5461}$ +15·6° in CS_2 (*c*, 5·70); [8, 9] Ethers formed. [10] Esters insoluble in cold *cyclo*hexane.

TABLE V.

Transformation of (—)α-Phenyl-γ-methylallyl Hydrogen Phthalate into (+)γ-Phenyl-α-methylallyl Hydrogen Phthalate at Room Temperature in Carbon Disulphide (l, 2).

Time, hours.	(*c*, 1·5.) α_{5461}.	α_{4358}.	(*c*, 3·0.) α_{5461}.	α_{4358}.	Time, hours.	(*c*, 1·5.) α_{5461}.	α_{4358}.	(*c*, 3·0.) α_{5461}.	α_{4358}.
0	+0·10°	+0·21°	+0·20°	+0·43°	94	+0·47°	+0·86°	+1·00°	+2·01°
19	0·18	0·38	0·39	0·81	111	0·52	0·89	1·12	2·27
43	0·26	0·57	0·59	1·10	163	0·56	1·14	1·18	2·50
67	0·39	0·76	0·90	1·63	212	0·56	1·08	1·18	2·50

TABLE VI.

Influence of Temperature on the Rate of Change of (—)α-Phenyl-γ-methylallyl Hydrogen Phthalate into (+)γ-Phenyl-α-methylallyl Hydrogen Phthalate in Benzene Solution.

At 18°. *c*, 3·060; *l*, 2.		At 37°. *c*, 4·85; *l*, 2.		At 47°. *c*, 5·0; *l*, 2.		At 55°. *c*, 5·0; *l*, 2.	
t, hrs.	$\alpha^{18°}_{5461}$.	*t*, mins.	$\alpha^{37°}_{5461}$.	*t*, mins.	$\alpha^{47°}_{5461}$.	*t*, mins.	$\alpha^{55°}_{5461}$.
0	−0·74°	0	−0·88°	0	−0·47°	0	0·0°
19·5	0·43	10	0·85	6	0·42	3	+0·15
72·5	0·12	30	0·72	22	0·26	5	0·21
91·5	+0·02	60	0·57	48	0·02	10	0·35
236	0·16	90	0·47	60	0·00	15	0·46
308	0·20	180	0·15	70	+0·05	20	0·52
		210	0·00	95	0·12	25	0·52
$10^4 k$ = 0·39 (time units in minutes)		5·75		23		115	

The salts of (—)α-phenyl-γ-methylallyl hydrogen phthalate showed far less tendency to undergo isomeric change than did the acid ester. The rotatory power, $[\alpha]^{20°}_{5461}$ + 11·0°, (*c*, 2·25; *l*, 2), of a solution of the hydrogen phthalic ester in ether containing ammonia remained unchanged during 9 days, after which the solution became cloudy, making accurate readings difficult: (+)γ-phenyl-α-methylallyl hydrogen phthalate under the same conditions had $[\alpha]_{5461}$ + 44·0° (*c*, 1·50; *l*, 2). Similarly, the quinidine salt of the (—)α-phenyl ester remains unchanged for many months, whilst the ester is quite stable in cold pyridine solution (see Table IV).

The relative stability of the hydrogen phthalic ester in pyridine solution is of particular interest because in the preparation of the ester by the action of a pyridine solution of phthalic anhydride on the alcohol it was found that unless the temperature of the reaction was kept below 45° the product consisted almost entirely of γ-phenyl-α-methylallyl hydrogen phthalate. It thus appears that in the course of its preparation the α-phenyl ester passes through a phase which favours its isomeric change.

A similar observation was made with the *p*-xenylurethane of the α-phenyl alcohol, which like the hydrogen phthalic ester readily underwent isomeric change. When (—)α-phenyl-γ-methylallyl alcohol and *p*-xenyl *iso*cyanate were mixed in molecular proportion and heated at 40—45° for 2·5 hours, (+)α-phenyl-γ-methylallyl *p*-xenylurethane with $[\alpha]_{5461}$ + 24·4° in chloroform was obtained. It was maintained molten (120°) for a few minutes, kept in boiling benzene solution for 4 hours, and kept in benzonitrile solution for 14 days at room temperature without its rotatory power, $[\alpha]_{5790}$ + 5·4°, $[\alpha]_{5461}$ + 7·3° (*c*, 1·30; *l*, 2), undergoing any change. On the other hand, when the original mixture of (—)alcohol and *iso*cyanate was heated on a steam-bath for ½ hour the solid product consisted entirely of (+)γ-phenyl-α-methylallyl *p*-xenylurethane, which after one crystallisation from benzene had $[\alpha]_{5461}$ + 175·4° in chloroform. Although some dl-*urethane* may have been removed during the crystallisation (the *dl*-urethane is not very soluble in benzene) this reaction is remarkable for the very high proportion, *i.e.*, 87·7%, of optical activity which survived the isomeric change.

The neutral esters of (—)α-phenyl-γ-methylallyl alcohol were more stable than the acid phthalic ester. The *p*-nitrobenzoic esters of the *dl*- and the (—)-alcohol were prepared in a pure condition with little difficulty (compare Burton, *loc. cit.*): the *dl*- and (+)-γ-phenyl-α-methylallyl *p*-nitrobenzoates have already been described (Kenyon, Partridge, and Phillips, *loc. cit.*). A specimen of dl-*α-phenyl-γ-methylallyl* p-*nitrobenzoate* changed but slightly when kept for a year in a closed bottle, and resolidified unchanged after being kept molten for ½ hour. After being kept at 100° for 2·5 hours it solidified immediately when inoculated with a crystal of *dl*-γ-phenyl-α-methylallyl *p*-nitrobenzoate, the crystalline mass having m. p. 46—48° before recrystallisation, and after recrystallisation m. p. 58—59° either alone or mixed with authentic *dl*-γ-phenyl-α-methylallyl *p*-nitrobenzoate. The (—)ester after similar treatment was separated by crystallisation into *dl*- and (—)-γ-phenyl-α-methylallyl *p*-nitrobenzoates; the latter ester had $[\alpha]_{5461}$ — 15·7° in chloroform; whereas the optically pure (—)-γ-ester had $[\alpha]_{5461}$ — 33·5° in this solvent. In solution the *p*-nitrobenzoate is more stable than the hydrogen phthalic ester, as is shown by the data given in Table VII.

The acetate of (−)α-phenyl-γ-methylallyl alcohol, prepared by the action of acetic acid-free acetic anhydride on a solution of the (−)α-phenyl alcohol in pyridine, was converted by acetic acid at room temperature into (+)γ-phenyl-α-methylallyl acetate (Kenyon, Partridge, and Phillips, *loc. cit.*), the rotatory power of the solution changing from $[\alpha]_{5461}$ + 3·0° to a maximum value of $[\alpha]_{5461}$ + 28·9° in 17 hours. After 54 hours (+)γ-phenyl-α-methylallyl acetate was isolated from the solution with $\alpha_{5461}^{26\cdot5^\circ}$ + 11·69° (*l*, 0·5), a value which is 14·1% of that of the optically pure (+)γ-phenyl-α-methylallyl acetate.

Stereochemical Aspects of the Anionotropic Changes and Replacement Reactions undergone by (−)α-Phenyl-γ-methylallyl Alcohol and its Derivatives.—A summary of the anionotropic changes studied is given in Fig. 1 (p. 214), which includes also reactions in which the anionic groups of the *p*-nitrobenzoic and hydrogen phthalic esters of (−)α-phenyl-γ-methylallyl alcohol were replaced by the anions –OAc and –OMe, by heating the esters with acetic acid and methyl alcohol respectively. From this scheme it will be seen that if the relative configurations of (+)phenyl-*n*-propyl- and (−)β-phenylethylmethyl-carbinols were known, it would be possible to deduce which of these changes were accompanied by inversion and which took place without configurative changes.

The relative configurations of these two alcohols can be decided from data already published if use is made of generalisations which have emerged from studies with optically active compounds. These include the experimental results of Pickard and Kenyon (J., 1911, **99**, 45, *et seq.*) on the determination of the rotatory powers of homologous series of alcohols and their esters, the work of Clough (J., 1918, **113**, 536, *et seq.*) showing that the rotatory powers of compounds of similar configuration are in general influenced similarly by changes in external conditions, and the investigations of Rule (J., 1924, **125**, 1121, *et seq.*) on the

TABLE VII.

Transformation of (−)α-Phenyl-γ-methylallyl p-*Nitrobenzoate into (−)γ-Phenyl-α-methylallyl* p-*Nitrobenzoate.*

				Initial values.			Final values.		
Solvent.	*t*.	Time.	*c*.	$[\alpha]_{5790}$.	$[\alpha]_{5461}$.	$[\alpha]_{4358}$.	$[\alpha]_{5790}$.	$[\alpha]_{5461}$.	$[\alpha]_{4358}$.
C_6H_6 *	82°	3·5 hrs.	4·0	−39·7°	−44·0°	—	−30·0°	−36·0°	—
$CHCl_3$ †	15—20	3 months	4·6	−39·4	−45·0	−83·4°	0·0	0·0	0·0°
C_5H_5N	15	2 ,,	2·7	−46·3	−51·9	—	−46·3	−51·9	—
Et_2O	15	2 ,,	3·6	−34·0	−38·9	−73·6	−34·0	−38·9	−73·6
Et_2O + 1 drop conc. HCl	15	2 days	3·6	−34·0	−38·9	−73·6	−29·4	−34·0	—

* The recovered ester remained liquid.

† The recovered ester had m. p. 46—50° and was mainly *dl*-γ-phenyl-α-methylallyl *p*-nitrobenzoate.

influence of the polarity of the substituent, X, on the magnitude of the rotatory powers of compounds of the series RX. From these investigations it can be concluded that the rotatory powers of the series of alcohols, Ph·CH(OH)·R, in which R is a lengthening alkyl chain, and also of the series, Me·CH(OH)·R, in which R contains a phenyl group becoming separated from the asymmetric carbon atom by an increasing number of methylene groups, should alter in a regular manner. The experimentally determined rotatory powers of some of the alcohols belonging to these two series both in the homogeneous state and also in benzene solution for light of three different wave-lengths are given in Table VIII.

It will be seen that the rotatory powers of the (+)alcohols of the second series (1, 4, and 5) steadily decrease in magnitude both in the homogeneous state and in benzene solution. The decrease in the rotatory powers of the first series (1, 2, and 3) is not so regular, (+)phenylethylcarbinol, the middle member of the series, having slightly lower rotatory powers than either phenylmethyl- or phenyl-*n*-propyl-carbinol. This small irregularity is not serious, however, since the lack of simplicity in the rotatory dispersive powers of these alcohols makes a comparison under strictly comparable conditions difficult. (+)Phenylmethylcarbinol thus appears to be configuratively related to the alcohols of both series, and hence all the five alcohols have the same configuration. Confirmation of this conclusion is afforded by a comparison of the temperature–rotation curves of these alcohols (Pickard and

Kenyon; Kenyon and Partridge, *locc. cit.*). All five alcohols give temperature–rotation curves which tend to be concave to the temperature axis.

TABLE VIII.

The Specific Rotatory Powers of Related Semiaromatic Alcohols.

	$[\alpha]_{\lambda}^{20°}$. Homogeneous state. λ.			$[\alpha]_{\lambda}^{17-20°}$. In benzene (*c*, 5·00). λ.		
	5893.	5461.	4358.	5893.	5461.	4358.
1. Ph·CH(OH)Me *	+41·51°	+49·46°	+85·92°	+48·88°	+57·93°	+99·22°
2. Ph·CH(OH)·CH_2Me *	+30·24	+36·02	+60·49	+40·05	+47·78	+79·16
3. Ph·CH(OH)·CH_2Et †	—	+36·58	+63·00	+43·60	+52·20	+87·30
4. CH_2Ph·CH(OH)Me *	+27·58	+33·43	+61·22	+41·82	+50·82	+93·58
5. CH_2Ph·CH_2·CH(OH)Me *	+14·74	+17·46	+29·28	+19·41	+25·45	+42·79

* Pickard and Kenyon, J., 1914, **105**, 1110.

† From data given by Kenyon and Partridge, J., 1936, 128.

From these considerations it follows that (+)phenyl-*n*-propylcarbinol has the same configuration as (+)β-phenylethylmethylcarbinol, and since the two unsaturated alcohols were reduced by the same method, it can be concluded that (—)α-phenyl-γ-methylallyl alcohol has a configuration opposite to that of (+)γ-phenyl-α-methylallyl alcohol. Hence the new asymmetric centre produced by the isomeric change of (—)α-phenyl-γ-methylallyl alcohol *has the opposite configuration to the asymmetric centre which is destroyed.*

Furthermore, since the hydrogen phthalic, acetic, and *p*-nitrobenzoic esters are produced from the unsaturated alcohols by methods unlikely to lead to configurative change, the isomeric change of these esters of the α-phenyl alcohol into the corresponding esters of the γ-phenyl alcohol is accompanied by inversion of configuration.

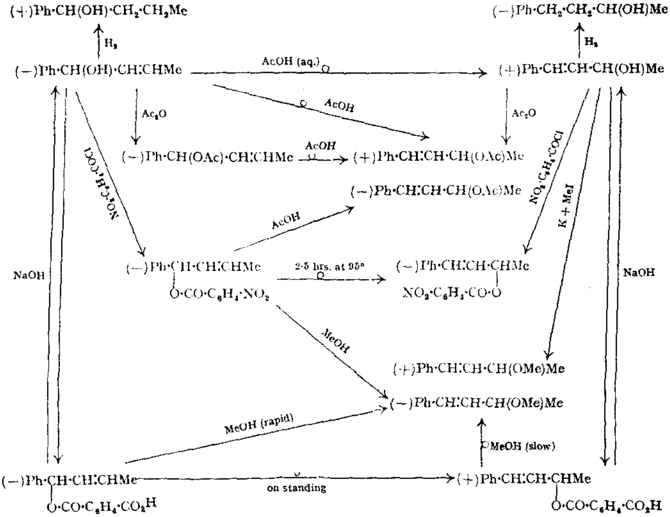
Other conclusions can be drawn concerning the stereochemical changes which occur during reactions given in the scheme. For example, it can be assumed that the (+)*γ-phenyl-α-methylallyl methyl ether* produced from the potassio-derivative of the (+)alcohol by the action of methyl iodide possesses the same configuration as the parent (+)alcohol and also its (+)hydrogen phthalic ester. The (—)γ-phenyl-α-methylallyl methyl ether *slowly* produced when the (+)hydrogen phthalic ester was warmed with methyl alcohol arose, therefore, with inversion of configuration. On the other hand, if, as suggested, (—)α-phenyl-γ-methylallyl hydrogen phthalate and (—)α-phenyl-γ-methylallyl *p*-nitrobenzoate have a configuration opposite to that of (+)γ-phenyl-α-methylallyl hydrogen phthalate and (—)γ-phenyl-α-methylallyl *p*-nitrobenzoate, then they must have the same configuration as (—)γ-phenyl-α-methylallyl methyl ether. Hence both these esters undergo anionic replacement without the occurrence of inversion of configuration. It is also noteworthy that both these esters react *rapidly* with methyl alcohol: the anionic replacements are unlikely therefore to have been preceded by isomeric change, since the corresponding γ-phenyl esters react *slowly* with methyl alcohol.

The proposed configurational relationships between the compounds produced as indicated in Fig. 1 fit in with a relatively simple picture of the reaction mechanism. This is provided by assuming that *the (—)α-phenyl-γ-methylallyl esters adopt a pseudo-cyclic* configuration (see Fig. 2), in which the *cis*-form predominates. The arrangement of the groups around the γ-carbon atom will then be favourable to the adoption of a (+)configuration, *i.e.*, opposite to that of the α-asymmetric carbon atom, when the anion migrates.

Isomerisation involves, then, the establishment of a link between the carboxyl oxygen atom and the γ-carbon atom, as indicated by the broken line; complete migration of the anion involves inversion of configuration. Anionic migration may be forestalled, however, by union of the γ-carbon atom with an external anion, *e.g.*, –OMe. When this occurs, as indicated by the dotted line, the new asymmetric centre acquires the same configuration as that previously possessed by the α-carbon atom. On the other hand, when the internal anion is attached to the γ-carbon atom and shows no tendency to migrate, but can nevertheless undergo displacement by an external anion, as when (+)γ-phenyl-α-methylallyl

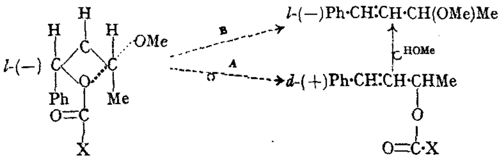
hydrogen phthalate is converted into (+)γ-phenyl-α-methylallyl *methyl* ether, then a Walden inversion occurs as in most other simple anionic replacement reactions.

FIG. 1.



In view of the fact that this picture of the space-mechanism of the isomerism and of the replacement reaction assumes the proximity of the ester-oxygen atom and the γ-carbon atom, it is of interest that α-phenyl-γ-methylallyl alcohol has a low parachor (360·6), whilst the parachor of γ-phenyl-α-methylallyl alcohol (367·4) is nearer the calculated value, which is 372·1 according to the constants of Sugden ("The Parachor and Valency," p. 38), or 368·2 according to those of Mumford and (J. W. C.) Phillips (J., 1929, 2113).

FIG. 2.



$X = -C_6H_4{\cdot}CO_2H(o\text{-})$ or $-C_6H_4{\cdot}NO_2(p\text{-})$

(*l*- and *d*- denote configurations.)

If such a pseudo-cyclic configuration is adopted by anionotropic systems prior to anion migration, then a mechanism is provided by which an external anion can become attached to the γ-carbon atom of α-phenyl-γ-methylallyl alcohol without postulating the occurrence of complete ionic dissociation prior to isomeric change. This is a modification of the views

of Burton (*loc. cit.*), who assumed that the formation of cinnamyl acetate resulting from the action of tetramethylammonium acetate on α-phenylallyl *p*-nitrobenzoate in acetic anhydride indicated that ionic dissociation proceeded sufficiently far to permit of direct competition between the internal and external anions for the electromeric cation. Our interpretation would, however, appear to be more in accord with the conclusions reached by Hsü, Ingold, and Wilson (J., 1935, 1778), from their studies of prototropic systems, namely, that the ionisation products of the system do not become kinetically free to such a degree as to allow of asymmetry being destroyed.

EXPERIMENTAL.

The phenylurethane of *dl*-α-phenyl-γ-methylallyl alcohol (b. p. 121—122°/12 mm., $n_D^{20°}$ 1·5525; Burton, *loc. cit.*) failed to crystallise, but its p-*xenylurethane* (0·8 g.), prepared by warming together for 2·5 hours at 40—45° *p*-xenyl *iso*cyanate (1 g.) and the alcohol (0·7 g.), separated from light petroleum and ether in radiating clusters of prismatic needles, m. p. 124° (Found : N, 4·25. $C_{23}H_{21}O_2N$ requires N, 4·1%).

dl-α-*Phenyl-γ-methylallyl* p-*nitrobenzoate* (20 g.), prepared by the interaction of the alcohol (14·8 g.) and *p*-nitrobenzoyl chloride (18·8 g.) in the presence of pyridine (10 g.), crystallised from a mixture of ether and light petroleum in radiating clusters of almost colourless, prismatic needles, m. p. 99° (Found : N, 4·8. $C_{17}H_{15}O_4N$ requires N, 4·7%). Mixed with *dl*-γ-phenyl-α-methylallyl *p*-nitrobenzoate (m. p. 58—59°), it melts very indefinitely at 45—75°. dl-α-*Phenyl-γ-methylallyl acetate* (6·8 g.), b. p. 135—136°/21·5 mm., $n_D^{25°}$ 1·5087 (Found : C, 75·5; H, 7·4. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·4%), was readily obtained by the action of acetic anhydride (5·4 g., freed from acetic acid by Meisenheimer and Beutter's method, *Annalen*, 1934, **508**, 70) on a warm mixture of the alcohol (6·0 g.) and pyridine (5·0 g.).

dl-α-*Phenyl-γ-methylallyl hydrogen phthalate.* A solution of phthalic anhydride (30 g.) in hot pyridine (60 g.) was rapidly cooled and mixed with *dl*-α-phenyl-γ-methylallyl alcohol (30 g.); the resultant mixture was maintained at 40—45° for 2 hours and occasionally shaken. The homogeneous liquid was dissolved in ether and washed repeatedly with ice-cold dilute hydrochloric acid. When most of the ether had been removed by the aqueous acid, the hydrogen phthalic ester began to crystallise. On addition of a large volume of cold water, followed by vigorous shaking, it separated completely as small granules. These were finely triturated with cold dilute hydrochloric acid, filtered, washed with water, and dried in a vacuum, m. p. 77—79°; yield 54 g. dl-α-*Phenyl-γ-methylallyl hydrogen phthalate* separated from a mixture of ether and light petroleum in small needles, m. p. 93—94° (Found : C, 72·65; H, 5·4. $C_{18}H_{16}O_4$ requires C, 73·0; H, 5·4%); mixed with *dl*-γ-phenyl-α-methylallyl hydrogen phthalate, it softened and melted at 92—94°. When saponified with alcoholic sodium hydroxide, the alcohol obtained distilled sharply at 119—120°/9·5 mm., and since it could not be induced to solidify, was relatively free from γ-phenyl-α-methylallyl alcohol (m. p. 33°). Very little transformation of the hydrogen phthalic ester to γ-phenyl-α-methylallyl hydrogen phthalate could therefore have occurred during either its preparation or saponification.

If, during the preparation of the ester, the precautions described above, particularly the avoidance of high temperature, were not taken, the product was not homogeneous. When a mixture of alcohol, phthalic anhydride, and pyridine was heated on the steam-bath for an hour complete transformation occurred, and the product consisted of the isomeric *dl*-γ-phenyl-α-methylallyl hydrogen phthalate, m. p. and mixed m. p. 92—94°, giving *dl*-γ-phenyl-α-methylallyl alcohol, m. p. 30—31·5°, when saponified.

Quinidine Salt of (−)α-*Phenyl-γ-methylallyl Hydrogen Phthalate.*—When quinidine (24 g.) was dissolved in a cold solution of *dl*-α-phenyl-γ-methylallyl hydrogen phthalate (22 g.) in methyl acetate (300 c.c.), a bulky mass of asbestos-like crystals separated immediately. These, after recrystallisation from methyl acetate (2300 c.c.), consisted of the optically pure quinidine salt of (−)α-phenyl-γ-methylallyl hydrogen phthalate (18·5 g.), m. p. 146—147° (decomp.).

Quinidine Salt of (+)α-*Phenyl-γ-methylallyl Hydrogen Phthalate.*—The filtrate from the quinidine salt, described above, after removal of the solvent yielded a gum (16 g.), which dissolved readily in hot acetone (60 c.c.). After cooling, this solution deposited bulky clusters of silky needles which, when recrystallised from acetone (60 c.c.), gave the quinidine salt of (+)α-phenyl-γ-methylallyl hydrogen phthalate (4·3 g.), m. p. 133—134° (decomp.).

(−)α-*Phenyl-γ-methylallyl Hydrogen Phthalate.*—The quinidine salt of m. p. 146—147° (62 g.), mixed with acetone (150 c.c.), was decomposed with ice-cold dilute hydrochloric acid, and the liberated hydrogen phthalic ester precipitated by addition of water and extracted with

ether. The dried ethereal solution, mixed with warm light petroleum, deposited (−)α-phenyl-γ-methylallyl hydrogen phthalate as rosettes of long, fine, glistening needles (23 g.), m. p. 81—82°.

(+)α-Phenyl-γ-methylallyl Hydrogen Phthalate.—The quinidine salt of m. p. 133—134° (4·3 g.), when decomposed by the method described in the preceding paragraph, yielded (+)α-phenyl-γ-methylallyl hydrogen phthalate (1·75 g.), glistening needles, m. p. 80—81°.

(−)α-Phenyl-γ-methylallyl alcohol was obtained by adding (−)α-phenyl-γ-methylallyl hydrogen phthalate (19 g.) to a hot solution of sodium hydroxide (6·5 g.) in alcohol (300 c.c.) and then passing steam through the mixture. The steam-distillate (900 c.c.) on extraction yielded (−)α-phenyl-γ-methylallyl alcohol (8·5 g.), b. p. 126°/20 mm., $n_D^{20°}$ 1·5525. Its *p*-xenylurethane, hairy needles, m. p. 120°, from methylene chloride and light petroleum, has $[\alpha]_{5893}$ + 20·0°, $[\alpha]_{5790}$ + 22·6°, $[\alpha]_{5461}$ + 24·4°, $[\alpha]_{4358}$ + 58·2° (*c*, 2·25; *l*, 2) in chloroform. When saponification was effected by a slight excess of aqueous 5*N*-sodium hydroxide, however, the liberated alcohol was a mixture, b. p. 122—128·5°/11 mm., from which by fractional distillation (+)γ-phenyl-α-methylallyl alcohol, m. p. 31°, $\alpha_{5461}^{20°}$ + 0·35° (*l*, 0·25), was isolated. Similarly, when aqueous alcoholic sodium carbonate was used, the liberated alcohols were separated by distillation into: (i) b. p. 119—121·5°/11 mm., $\alpha_{5461}^{20°}$ − 4·35° (*l*, 0·25), (ii) b. p. 128—129°/10 mm., $\alpha_{5461}^{20°}$ − 2·14° (*l*, 0·25). Fraction (ii), when inoculated with *dl*-γ-phenyl-α-methylallyl alcohol, deposited crystals of (+)γ-phenyl-α-methylallyl alcohol, m. p. 33—34°, $[\alpha]_{5461}$ + 2·2° (*c*, 4·6; *l*, 2) in pyridine solution.

(−)α-Phenyl-γ-methylallyl acetate, b. p. 134—135°/20 mm., $n_D^{26·5°}$ 1·5064, $d_{4°}^{22·5°}$ 1·016, $\alpha_{5893}^{23°}$ − 0·34°, $\alpha_{5461}^{23°}$ − 0·41°, $\alpha_{4358}^{23°}$ − 1·23° (*l*, 0·25), was prepared by warming at 60—70° for an hour a mixture of the (−)alcohol ($\alpha_{5461}^{20°}$ − 33·59°; *l*, 0·5; 3 g.), acetic acid-free acetic anhydride (2·7 g.), and pyridine (2·5 g.) (Found: C, 75·5; H, 7·8. $C_{12}H_{14}O_2$ requires C, 75·8; H, 7·4%).

(−)α-Phenyl-γ-methylallyl p-Nitrobenzoate.—A solution of *p*-nitrobenzoyl chloride (4 g.) in chloroform (15 c.c.) was added dropwise to a mixture of the (−)alcohol (3 g.) and pyridine (2 g.). The reaction mixture, which became warm, was left for 24 hours; the resulting *p*-nitrobenzoic ester was an oil, the rotatory powers of which are in Table VII.

Transformation of (−)α-Phenyl-γ-methylallyl Alcohol into (+)γ-Phenyl-α-methylallyl Alcohol.—A solution of (−)α-phenyl-γ-methylallyl alcohol (1·5 c.c.; $\alpha_{5461}^{20°}$ − 14·98°, *l*, 0·25) in 0·5% aqueous acetic acid (500 c.c.) after standing 40 hours at room temperature was rendered slightly alkaline and extracted with ether. The dried extract yielded (+)γ-phenyl-α-methylallyl alcohol, b. p. 140°/20 mm., which crystallised immediately when inoculated with an authentic specimen, m. p. 33°, α_{5893} + 0·51°, α_{5461} + 0·69°, α_{4358} + 1·36° (*l*, 0·5).

Freshly distilled *dl*-α-phenyl-γ-methylallyl alcohol, b. p. 125—126°/15 mm. (5 g.), was shaken for 15 hours with 20% aqueous acetic acid (50 c.c.) and worked up as described in the preceding paragraph. The resulting product distilled completely at 136—138°/16 mm. and, when inoculated with *dl*-γ-phenyl-α-methylallyl alcohol, set to a crystalline mass, m. p. 28—29°. Its *p*-xenylurethane (prepared below 65°), small needles from benzene, had m. p. 162—163° alone or mixed with an authentic specimen.

Conversion of Derivatives of α-Phenyl-γ-methylallyl Alcohol into Derivatives of γ-Phenyl-α-methylallyl Alcohol.—*Conversion of* dl-*α-phenyl-γ-methylallyl acetate into* dl-*γ-phenyl-α-methylallyl acetate.* (*a*) The acetate, b. p. 123°/11 mm. (5 g.), and acetic anhydride (7·5 g.) were heated together on the steam-bath for 10 hours and then distilled. After removal of acetic anhydride, the main portion distilled at 132—133°/9 mm.; this product (2·5 c.c.) was heated under reflux for 1·5 hours with aqueous-alcoholic sodium hydroxide and subsequently removed in a current of steam. The volatile material, b. p. 123—124°/8·5 mm., crystallised completely when inoculated with *dl*-γ-phenyl-α-methylallyl alcohol and had m. p. 30—31°. (*b*) The acetate (5 g.) was heated with glacial acetic acid (5 g.) on the steam-bath for 2 hours; the main portion (3·5 g.) then had b. p. 133—134°/10 mm., and after saponification (as above) yielded *dl*-γ-phenyl-α-methylallyl alcohol (2 c.c.), b. p. 125—126°/9·5 mm., m. p. 30—31°.

Conversion of (−)α-phenyl-γ-methylallyl acetate into (+)γ-phenyl-α-methylallyl acetate. The (−)acetate, $\alpha_{5461}^{23°}$ − 0·41° (*l*, 0·25), was dissolved in pure acetic acid, and the freshly prepared solution had $[\alpha]_{5893}$ + 2·6°, $[\alpha]_{5461}$ + 3·0°, $[\alpha]_{4358}$ + 4·2° (*c*, 5·10; *l*, 2). After this solution had stood for 17 hours at room temperature, its rotatory powers had changed to $[\alpha]_{5893}$ + 25·5°, $[\alpha]_{5461}$ + 28·9°, $[\alpha]_{4358}$ + 56·8°—values which remained unchanged after an additional 45 hours' standing. The isomeric (+)γ-phenyl-α-methylallyl acetate, prepared from (+)γ-phenyl-α-methylallyl alcohol (Kenyon, Partridge, and Phillips, J., 1936, 85), has $[\alpha]_{5893}$ + 145·0°, $[\alpha]_{5461}$ + 166·0°, $[\alpha]_{4358}$ + 321° (*c*, 1·12; *l*, 2) in acetic acid solution; hence the acetate formed by isomeric change of (−)α-phenyl-γ-methylallyl acetate in acetic acid possesses a rotatory power 17·2% of that of optically pure (+)γ-phenyl-α-methylallyl acetate. After removal of acetic acid the

residual (+)γ-phenyl-α-methylallyl acetate had b. p. 150—151°/22 mm., $n_D^{26\cdot5°}$ 1·525 and $\alpha_{5461}^{26\cdot5°}$ + 11·69°, $\alpha_{4358}^{26\cdot5°}$ + 22·86° (*l*, 0·5). The value $\alpha_{5461}^{26\cdot5°}$ + 11·69° is 14·1% of that of optically pure (+)γ-phenyl-α-methylallyl acetate.

Conversion of (−)α-phenyl-γ-methylallyl alcohol into (+)γ-phenyl-α-methylallyl acetate. A mixture of (−)α-phenyl-γ-methylallyl alcohol (3 g.; $\alpha_{5461}^{20°}$ − 14·98°; *l*, 0·25) and acetic acid (10 g.) after 4 days' standing at room temperature yielded (+)γ-phenyl-α-methylallyl acetate, b. p. 151°/24 mm., $\alpha_{5461}^{20°}$ + 1·74°, $\alpha_{4358}^{20°}$ + 3·6° (*l*, 0·5).

Conversion of (+)α-phenyl-γ-methylallyl alcohol into (−)γ-phenyl-α-methylallyl acetate. A specimen of optically impure (+)α-phenyl-γ-methylallyl alcohol ($\alpha_{5461}^{18°}$ + 4·47°; *l*, 0·25; $n_D^{20°}$ 1·5525), mixed with an equal weight of pure acetic anhydride, was heated on the steam-bath for 6·5 hours and then distilled. The main fraction had b. p. 136—138°/15 mm. and $\alpha_{5461}^{18°}$ − 3·26°, $\alpha_{4358}^{18°}$ − 6·25° (*l*, 0·25), $n_D^{20°}$ 1·5324, and was accordingly partially racemised (see above) (−)γ-phenyl-α-methylallyl acetate. That the loss of optical activity was not due to the action of acetic anhydride on the (−)γ-phenyl-α-methylallyl acetate produced was proved by heating a specimen of this acetate (with $\alpha_{5461}^{17°}$ − 9·88°; *l*, 0·5) with an equal weight of acetic anhydride for 8·5 hours on the steam-bath; when recovered it had $\alpha_{5461}^{15\cdot5°}$ − 10·52° (*l*, 0·5), $n_D^{15\cdot5°}$ 1·5310.

Transformation of α-Phenyl-γ-methylallyl p-*Nitrobenzoate into γ-Phenyl-α-methylallyl* p-*Nitrobenzoate.* (a) *In the homogeneous state.* A specimen of *dl*-α-phenyl-γ-methylallyl *p*-nitrobenzoate, m. p. 99°, after keeping in a closed vessel for a year had m. p. 96—97°; the amount of impurity (γ-phenyl-α-methylallyl *p*-nitrobenzoate ?) present was insufficient for separation by fractional crystallisation. The recrystallised ester after being kept molten for ½ hour resolidified unchanged to a crystalline mass, m. p. 98—99°; when, however, the molten material was kept at 100° for 2·5 hours, the cooled liquid did not solidify when inoculated with the original material but did so immediately when inoculated with *dl*-γ-phenyl-α-methylallyl *p*-nitrobenzoate and had m. p. 46—48°; after recrystallisation from ether and light petroleum, it had m. p. 58—59° alone or admixed with authentic *dl*-γ-phenyl-α-methylallyl *p*-nitrobenzoate.

(−)α-Phenyl-γ-methylallyl *p*-nitrobenzoate, after being kept at 100° for 2·5 hours, readily solidified on cooling and then had $[\alpha]_{5461}$ − 14·0°, $[\alpha]_{4358}$ − 33·7° (*c*, 3·65; *l*, 2) in chloroform. Crystallisation resolved this material into two fractions: (i) m. p. 50—52°, which when mixed with *dl*-γ-phenyl-α-methylallyl *p*-nitrobenzoate (m. p. 58°) melted at 57—58°, and (ii) a more soluble portion, m. p. 45°, which when mixed with (−)γ-phenyl-α-methylallyl *p*-nitrobenzoate (m. p. 41°) melted at 42—44°, and had $[\alpha]_{5790}$ − 13·8°, $[\alpha]_{5461}$ − 15·7°, $[\alpha]_{4358}$ − 38·5° (*c*, 1·07; *l*, 2) in chloroform. Optically pure (−)γ-phenyl-α-methylallyl *p*-nitrobenzoate has $[\alpha]_{5790}$ − 27·52°, $[\alpha]_{5461}$ − 33·48°, $[\alpha]_{4358}$ − 87·4° (*c*, 5·00; *l*, 2) in chloroform.

(b) *In solution.* By heating *dl*-α-phenyl-γ-methylallyl *p*-nitrobenzoate with 1·5 times its weight of acetic anhydride for 6 hours (3·5 hours were insufficient) on the steam-bath, it was converted into *dl*-γ-phenyl-α-methylallyl *p*-nitrobenzoate, m. p. and mixed m. p. 57—58°. About 5% of *p*-nitrobenzoic acid was isolated from the reaction mixture. Other data are recorded in Table VII.

Transformation of α-Phenyl-γ-methylallyl Hydrogen Phthalate into γ-Phenyl-α-methylallyl Hydrogen Phthalate.—*dl*-α-Phenyl-γ-methylallyl hydrogen phthalate was heated with an equal weight of pyridine on the steam-bath for an hour and the cooled solution mixed with cold dilute hydrochloric acid. The liberated oil soon crystallised, m. p. 94—95°, either alone or admixed with authentic *dl*-γ-phenyl-α-methylallyl hydrogen phthalate; it crystallised from carbon disulphide and light petroleum in characteristic, large, glassy rhombs, and on saponification gave *dl*-γ-phenyl-α-methylallyl alcohol, m. p. 30—31°.

Preparation of (+)γ-Phenyl-α-methylallyl Methyl Ether by a Method unlikely to lead to Inversion of Configuration.—Potassium (3·9 g.) was dissolved in an ethereal solution of (optically impure) (+)γ-phenyl-α-methylallyl alcohol, $[\alpha]_{5893}$ + 10·7° in carbon disulphide, and the resulting solution mixed with methyl iodide (14·5 g.) and gently warmed. The resulting (+)*γ-phenyl-α-methylallyl methyl ether* (1·5 g.) had b. p. 102—103°/10·5 mm., $\alpha_{5893}^{18°}$ + 6·61°, $\alpha_{5461}^{18°}$ + 7·92°, $\alpha_{4358}^{18°}$ + 13·93° (*l*, 0·25), $n_D^{18°}$ 1·5327. (Found: C, 82·0; H, 9·0. $C_{11}H_{14}O$ requires C, 81·5; H, 9·0%). Attempts to prepare the isomeric methyl ether from α-phenyl-γ-methylallyl alcohol by a similar procedure were unsuccessful.

Conversion of (+)γ-Phenyl-α-methylallyl Hydrogen Phthalate into (−)γ-Phenyl-α-methylallyl Ethyl Ether.—(+)γ-Phenyl-α-methylallyl hydrogen phthalate (14·90 g.), made up to 100 c.c. with absolute ethyl alcohol, had $[\alpha]_{5893}$ − 12·3°, $[\alpha]_{5790}$ − 12·9°, $[\alpha]_{5461}$ − 14·7°, $[\alpha]_{4358}$ − 28·2° (*c*, 14·9; *l*, 2), and after 24 days' keeping at room temperature, $[\alpha]_{5461}$ − 14·1°. After 9 months' keeping at 25° the rotatory power had reached the constant value $[\alpha]_{5461}$ − 1·5°, the half-life period being about 60 days. This solution yielded (−)*γ-phenyl-α-methyllalyl ethyl ether* (7 g.),

b. p. 114°/11 mm., $n_D^{17°}$ 1·5262, $\alpha_{5893}^{18°}$ − 2·20°, $\alpha_{5461}^{18°}$ − 2·50° (*l*, 2) (Found: C, 82·1; H, 9·1. $C_{12}H_{16}O$ requires C, 81·8; H, 9·1%).

Conversion of (+)*γ-Phenyl-α-methylallyl Hydrogen Phthalate into* (−)*γ-Phenyl-α-methylallyl Methyl Ether*.—The hydrogen phthalate (14·60 g.), made up to 100 c.c. with methyl alcohol (distilled from calcium), had $[\alpha]_{5893}$ − 7·2°, $[\alpha]_{5790}$ − 7·4°, $[\alpha]_{5461}$ − 8·4°, $[\alpha]_{4358}$ − 15·3° (*c*, 14·6; *l*, 2), and after being kept for 30 days at room temperature, $[\alpha]_{5461}$ − 6·3°. After a further 3 months the constant value $[\alpha]_{5461}$ − 72° was reached, half-life period about 34 days, and from the solution, which contained no unchanged hydrogen phthalic ester, (−)γ-phenyl-α-methylallyl methyl ether (7·5 g.), b. p. 124°/25 mm., $n_D^{17°}$ 1·5337, $\alpha_{5893}^{24°}$ − 0·34°, $\alpha_{5461}^{24°}$ − 0·38°, α_{4358} − 0·59° (*l*, 0·25), was isolated. A second experiment showed that when the original solution was heated under reflux, the reaction was complete in 30 minutes, the resulting methyl ether having b. p. 103°/10 mm., $\alpha_{5893}^{19°}$ − 0·48° (*l*, 0·5), $n_D^{19°}$ 1·5325.

Conversion of (−)*α-Phenyl-γ-methylallyl Hydrogen Phthalate into* (−)*γ-Phenyl-α-methylallyl Methyl Ether*.—A solution of (−)α-phenyl-γ-methylallyl hydrogen phthalate in methyl alcohol (freshly distilled from calcium) (*c*, 5·292; *l*, 2) gave the following changes in rotatory power (all negative) on standing at room temperature.

Time, mins.	0	20	45	70	165	260	320	480	1660	3 days
α_{5893}	2·51°	—	2·31°	2·23°	—	—	—	0·72°	0·17°	—
α_{5790}	2·67°	—	2·43°	—	1·44°	1·38°	1·10°	0·75°	—	0·10°
α_{5461}	3·05°	2·95°	2·81°	2·72°	1·66°	1·51°	1·20°	0·85°	0·19°	0·12°
α_{4358}	6·20°	—	5·67°	—	3·92°	3·00°	2·57°	1·72°	0·37°	0·35°

After evaporation of the solvent, there were obtained phthalic acid and (−)γ-phenyl-α-methylallyl methyl ether, b. p. 118°/20 mm., $\alpha_{5790}^{20°}$ − 0·12°, $\alpha_{5461}^{20°}$ − 0·20°, $\alpha_{4358}^{20°}$ − 0·25° (*l*, 0·25), $n_D^{20°}$ 1·5322.

Transformations of (−)*α-Phenyl-γ-methylallyl* p-*Nitrobenzoate*.—(a) *Into* (−)*γ-phenyl-α-methylallyl acetate by the action of acetic acid at ordinary temperature.* A solution of (−)α-phenyl-γ-methylallyl *p*-nitrobenzoate in glacial acetic acid had $[\alpha]_{5790}$ − 41·1°, $[\alpha]_{5461}$ − 46·7°, $[\alpha]_{4358}$ − 93·2° (*c*, 4·45; *l*, 2) when freshly prepared and, after standing for 24 hours at room temperature, the constant values $[\alpha]_{5790}$ − 7·1°, $[\alpha]_{5461}$ − 7·5°, $[\alpha]_{4358}$ − 18·4°. From a parallel experiment using a larger amount (4 g.) of the *dl*-*p*-nitrobenzoate there was isolated *dl*-γ-phenyl-α-methylallyl acetate (1·5 g.), b. p. 147°/18 mm., $n_D^{19°}$ 1·534. Since optically pure (−)γ-phenyl-α-methylallyl acetate has $[\alpha]_{5461}$ − 166° in acetic acid (*c*, 1·12; *l*, 2), it follows that the replacement of the *p*-nitrobenzoyl group by the acetyl group has been effected with the maintenance of some 4·5% of the optical activity of the new ester.

(b) *Into* (−)*γ-phenyl-α-methylallyl methyl ether by the action of methyl alcohol at ordinary temperature*. A solution of (−)α-phenyl-γ-methylallyl *p*-nitrobenzoate in methyl alcohol had $[\alpha]_{5790}$ − 40·25°, $[\alpha]_{5461}$ − 47·0°, $[\alpha]_{4358}$ − 90·3° (*c*, 2·20; *l*, 2) when freshly prepared; after 6 days' standing the constant value $[\alpha]_{5461}$ − 5·23° was reached. From a parallel experiment using the *dl*-*p*-nitrobenzoate (5 g.) there were isolated *p*-nitrobenzoic acid (2·5 g.) and *dl*-γ-phenyl-α-methylallyl methyl ether (2·0 g.), b. p. 112°/15 mm., $n_D^{22°}$ 1·5321.

Conversion of (−)*α-Phenyl-γ-methylallyl Alcohol into* (+)*γ-Phenyl-α-methylallyl* p-*Xenylurethane*.—A mixture of (−)α-phenyl-γ-methylallyl alcohol (0·7 g.) and *p*-xenyl isocyanate (1 g.) was heated on the steam-bath for ½ hour. The resulting product, when crystallised from benzene, gave rosettes of hairy needles, (0·8 g.), $[\alpha]_{5790}$ + 147·6°, $[\alpha]_{5461}$ + 175·4°, $[\alpha]_{4358}$ + 369° (*c*, 2·25; *l*, 2) in chloroform, m. p. 176°; mixed with optically pure (+)γ-phenyl-α-methylallyl *p*-xenylurethane (m. p. 180°; $[\alpha]_{5461}$ + 200°, in chloroform) it melts at 182°.

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37. *An X-Ray Study of the Phthalocyanines. Part III. Quantitative Structure Determination of Nickel Phthalocyanine.*

By J. Monteath Robertson and Ida Woodward.

In a recent paper (J., 1936, 1195) it was shown that the phase constants of the *X*-ray reflections from crystals of phthalocyanine and its nickel derivative could be determined by comparing absolute measurements of the corresponding structure factors. This led to a direct metrical determination of the structure of the metal-free compound, by the method of Fourier analysis, with results in agreement with the chemical structure assigned by Linstead (J., 1934, 1016). Some small distortions from regularity were found to exist in the molecule, and it was thought these might be caused by internal hydrogen bonds connecting opposite pairs of *iso*indole nitrogen atoms. In order to obtain further information on this point and, in particular, to study the effect on the inner nucleus of the presence of a co-ordinating metal atom, we have now completed an independent Fourier analysis of the nickel phthalocyanine structure. Both structures have been verified by computing all the structure factors from the co-ordinates assigned to the atoms. These results are given in the experimental section (Table V).

The crystal data for nickel phthalocyanine, $C_{32}H_{16}N_8Ni$, are: space group C_{2h}^5 ($P2_1/a$), $a = 19{\cdot}9$, $b = 4{\cdot}71$, $c = 14{\cdot}9$ A., $\beta = 121{\cdot}9°$, with two centrosymmetrical molecules per unit cell of volume 1186 A.^{3}; d(found) = 1·63, (calc.) = 1·59, $M = 571$, $F(000) = 584$. The linear dimensions are almost identical with those of free phthalocyanine.

The method of finding the phase constants has already been described (*loc. cit.*, p. 1197), and in fact the determinations made for free phthalocyanine carry with them corresponding determinations for nickel phthalocyanine. It should be noted, however, that the results described below are derived from an entirely independent set of intensity measurements, made upon crystals of nickel phthalocyanine. The structure factors derived from these measurements, with the phase constants for the ($h0l$) zone, are collected in Table I.

Table I.

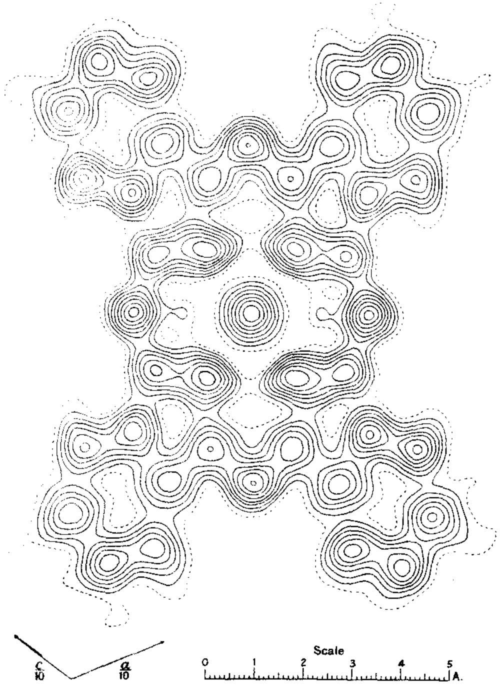
Values and Signs of $F(h0l)$.

l. \ h.	0	2	4	6	8	10	12	14	16	18	20
11	+ 16	—	—	—	—	—	—	—	—	—	—
10	+ 34	− 20	—	—	—	—	—	—	—	—	—
9	+ 17·5	—	+ 27	—	—	—	—	—	—	—	—
8	—	+ 38·5	+ 21·5	+33	—	—	—	—	—	—	—
7	+ 57	+ 51	+ 34·5	+78	+26	—	—	—	—	—	—
6	− 17·5	+ 25·5	+ 57·5	+50	+42	+16	—	—	—	—	—
5	− 12·5	− 29	—	+49·5	—	—	—	—	—	—	—
4	+ 55·5	+ 55·5	− 28	+43	+40·5	—	−15·5	—	—	—	—
3	—	+ 31	+ 46	—	+28·5	+35·5	+21·5	+18	—	—	—
2	− 36·5	+ 54	+ 49·5	−40	+49·5	—	—	+17·5	+24	—	—
1	+112	− 43	+ 28·5	—	+30·5	+26·5	+21·5	−15	—	—	—
0	+584	+ 55	—	+80·5	+44	+43·5	+40·5	+14·5	—	—	—
$\bar{1}$	+112	+136·5	+129	—	+58·5	+94·5	+38	+25	—	—	—
$\bar{2}$	− 36·5	+ 71·5	− 46	−10·5	+30	+50·5	+21·5	+25·5	+28·5	—	—
$\bar{3}$	—	+112·5	− 29·5	+ 9·5	+54·5	+60·5	+15	—	+16·5	+12·5	—
$\bar{4}$	+ 55·5	− 10·5	—	+44·5	+38	+44	+81	+14·5	—	+38	—
$\bar{5}$	− 12·5	+ 73·5	—	+24·5	+22	+17	+29·5	+35	+17	+36	—
$\bar{6}$	− 17·5	+ 37·5	+ 32·5	+65·5	+42	+59	−21·5	+39·5	+30·5	+14·5	+12·5
$\bar{7}$	+ 57	+ 50·5	+ 73	+56	+16	+31	—	+33	+26	+26·5	—
$\bar{8}$	—	+ 40·5	+ 91	+44·5	+67	−16·5	−12·5	—	+10	+11	—
$\bar{9}$	+ 17·5	+ 28	+ 35	—	+66·5	+40·5	—	−10	+33	—	—
$\bar{10}$	+ 34	+ 17	+ 38·5	+26·5	—	+32·5	+37·5	+24	+30	+16	+12·5
$\bar{11}$	+ 16	− 11·5	+ 26·5	+26	−14	+30·5	+25·5	—	+32·5	+16·5	—
$\bar{12}$	—	—	—	+22	—	—	+33	—	+14·5	—	—
$\bar{13}$	—	+ 41	—	—	+46	+38	+18	+15·5	+11·5	—	—
$\bar{14}$	—	—	—	—	—	+24·5	+36	+13·5	—	—	—

There are fewer absent reflections than in the metal-free compound. The great majority of those present are of positive sign, and the remaining negative values are all relatively small. This is due to the positive contribution made by the two nickel atoms to each reflection. Calculation shows that if the atomic number of the central metal atom were increased to about 60, all the structure factors would be of positive sign. This result

FIG. 1.

Projection of nickel phthalocyanine along the b *axis, which makes an angle of 44·2° with the molecular plane. Each contour line represents a density increment of one electron per A.², except on the central nickel atom, where the increment is five electrons per A.² for each line. The one-electron line is dotted.*

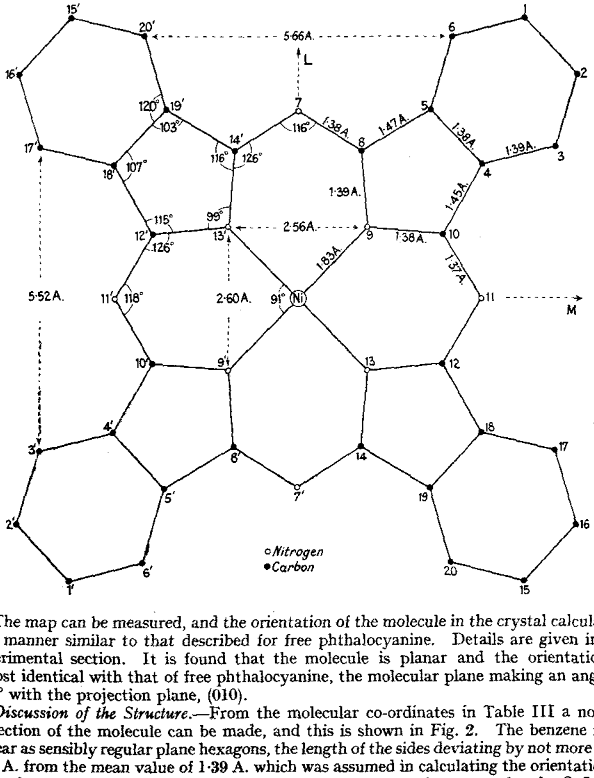


suggests a new method of direct analysis, *viz.*, by introducing an element at a known point in the structure of sufficient scattering power to "swamp" all the reflections. In a centro-symmetrical structure of the present type, the effect would be to convert all the structure factors to positive sign, and a direct Fourier analysis could be carried out. We hope to apply this method in a later investigation to find the orientation of the platinum phthalocyanine molecule in the crystal, which is not isomorphous with the other members of this series.

The result of the double Fourier synthesis for nickel phthalocyanine, with the figures of Table I as coefficients, is shown by the contoured map in Fig. 1 (which should be compared with Fig. 2 of the previous paper, *loc. cit.*, p. 1201). The resolution of the various atoms is quite equal to that obtained with free phthalocyanine, and the whole structure is closely similar, apart from the central nickel atom. On the nickel atom the contour levels, after the dotted one-electron line, are drawn at intervals of 5 electrons per A.^{2}, and the peak value of the density at the centre is 39 electrons per A.^{2}. This extreme peak, however, appears to have very little distorting effect on the surrounding structure.

FIG. 2.

Dimensions of the nickel phthalocyanine molecule.



The map can be measured, and the orientation of the molecule in the crystal calculated, in a manner similar to that described for free phthalocyanine. Details are given in the experimental section. It is found that the molecule is planar and the orientation is almost identical with that of free phthalocyanine, the molecular plane making an angle of 44·2° with the projection plane, (010).

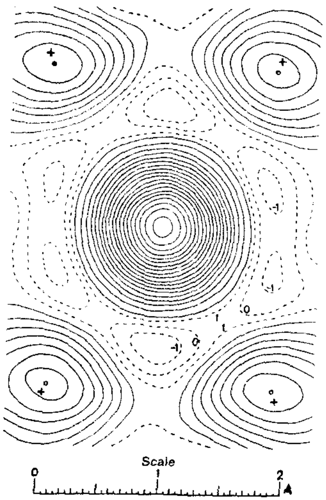
Discussion of the Structure.—From the molecular co-ordinates in Table III a normal projection of the molecule can be made, and this is shown in Fig. 2. The benzene rings appear as sensibly regular plane hexagons, the length of the sides deviating by not more than 0·04 A. from the mean value of 1·39 A. which was assumed in calculating the orientation of the molecule. These rings are connected to the inner carbon–nitrogen nucleus by C–C links of length 1·47 and 1·45 A. The corresponding links in free phthalocyanine gave the uniform

value of 1·49 A. The small contraction found for nickel phthalocyanine is practically within the limits of error (about 0·03 A.) and we should not attach much importance to this result.

The structure of the inner nucleus, however, shows certain changes compared with free phthalocyanine which, although not of large magnitude, are yet definitely beyond the limits of probable error which would arise from deficiencies in the experimental work or in the construction of the map. The largest of these is a shift of about 0·09 A. of each of the four *iso*indole nitrogen atoms towards the nickel atom to which they are bound by covalent or co-ordinate links. The movement is effected largely by a readjustment of the angles around the 16-membered C–N ring (compare with Fig. 3 of the previous paper). In particular, the angles at the apex (9,13) of the *iso*indole pentagons have decreased from 108° to 99°, while the side angles (8, 10, 12, 14) have increased by 4—6°.

FIG. 3.

Enlargement of central portion of molecule.



As a result of the inward displacement of the *iso*indole nitrogen atoms, their distance from the centre of the nickel atom is now only 1·83 A., compared with a corresponding value of 1·92 A. in the metal-free compound, measured from the nitrogen atoms to the centre of the molecule. It is interesting to note that this nickel–nitrogen distance of 1·83 A. is very close to the sum of the radii of neutral nickel (1·24 A.) and doubly-linked nitrogen (0·61 A.). When a larger metal atom, such as platinum (radius 1·38 A.), is substituted in the phthalocyanine molecule, it is probable that the inward displacement of the nitrogen atoms observed in the present structure will be diminished or even reversed (cf. Barrett, Dent, and Linstead, J., 1936, 1719).

In addition to these changes there is an interesting alteration in the dimensions of the C–N links in the nucleus itself. For free phthalocyanine these had the practically constant value of 1·33—1·34 A. In the present structure, the links 9—8 and 9—10, forming two sides of the *iso*indole pentagon, have increased in length to 1·38—1·39 A., a result which might to some extent have been anticipated in view of the strong covalent attachment of atom 9 to the central nickel atom. But the remaining links of the 16-membered ring, 8—7 and 10—11, although situated far from the nickel atom, have also increased in length to 1·38 and 1·37 A.; the net result being that *all the C–N links of the nucleus remain of practically equal length*, although about 0·04 A. longer than in free phthalocyanine.

It should be emphasised that this change in interatomic distance within the nucleus is of small order, and not much above the limit of uncertainty imposed by the incomplete resolution of the various atoms. The inward shift of the *iso*indole nitrogen atoms, amounting to 0·09 A., appears to be quite definite, but even here there are disturbing factors. These can best be studied by reference to Fig. 3, which gives an enlarged projection of the central portion of the molecule. The contour levels of the nickel atom are here drawn for density increments of 2 electrons per A.^{2}, the 1, 0, and − 1 levels are dotted, and all the other lines are at unit intervals. The roundness of the nickel atom indicates that there are no serious errors in the experimental work or in the calculations. The contours deviate

very slightly from true circles, although there is a small elongation in the direction of the *c* axis, a fact which may indicate a preferred direction in the thermal movements of the atom.

The four surrounding *iso*indole nitrogen atoms are shown at the corners of the diagram and the positions of the centres, obtained by averaging the four atoms and from other considerations, are indicated by small circles. The corresponding centres obtained from free phthalocyanine are shown by crosses. The inward shift of the atoms seems to be quite definite, and it might even be slightly greater than the amount we have given. There is, however, the difficulty of allowing for certain spurious undulations which may surround the nickel atom, due to the Fourier series being incomplete. Six small troughs will be observed, where the density drops to from − 1 to − 1·5 (as against a peak value at the centre of the nickel atom of 39). Further out, on a circle which will approximately pass through the *iso*indole nitrogen atoms, we might expect similar spurious *peaks*, and two such effects can be observed in Fig. 1, in line with the nitrogen atoms 11 and 11′. These effects, if present on the *iso*indole nitrogen atoms, might give a false impression of the positions of their centres, but we do not think they would explain the inward shift of the atoms that has been found. More abrupt distortions of the contour levels might be expected if such false detail were present on these atoms.

It is interesting to note that quite well-defined bridges exist in the direction of the covalent links connecting the nickel atom to the four nitrogen atoms (Fig. 3). The density in these regions is quite small, being only 0·5—0·7 electron per A.^{2}, but the result seems fairly definite as the bridges stand out above the adjacent negative portions.

In free phthalocyanine (J., 1936, 1205) it was shown that the molecule was slightly distorted from true tetragonal symmetry in a systematic manner which could be explained qualitatively by assuming that the distorting forces acted between the pairs of *iso*indole nitrogen atoms 9, 13′ and 13, 9′. To explain these forces, hydrogen-bond formation was assumed between the nitrogen atoms. We might expect that in nickel phthalocyanine these distortions would disappear and the molecule become truly tetragonal, owing to the more symmetrical distribution of the binding forces towards the central nickel atom.

The symmetry of the molecule can be tested in the same way as for free phthalocyanine, *viz.*, by comparing the lengths of horizontal and vertical lines connecting corresponding pairs of atoms, which would be equidistant if the molecules were exactly tetragonal. The measurements for nickel phthalocyanine are given (in A.) in Table II, with the differences in the lengths of corresponding lines, which give a measure of the departure from true tetragonal symmetry. The differences found for the free phthalocyanine molecule are also given for comparison.

TABLE II.

Test of Symmetry.

		Differences.	
Horizontal lines.	Vertical lines.	Nickel phthalocyanine.	Free phthalocyanine.
8, 14′ = 2·34	10, 12 = 2·36	−0·02	−0·03
9, 13′ = 2·56	9, 13 = 2·60	−0·04	−0·11
10, 12′ = 5·32	8, 14 = 5·38	−0·06	−0·14
11, 11′ = 6·72	7, 7′ = 6·84	−0·12	−0·22
1, 15′ = 8·36	2, 16 = 8·18	0·18	0·24
6, 20′ = 5·66	3, 17 = 5·52	0·14	0·19
2, 16′ = 10·30	1, 15 = 10·22	0·08	0·20
5, 19′ = 4·88	4, 18 = 4·87	0·01	0·08
3, 17′ = 9·47	6, 20 = 9·56	−0·09	0·08
4, 18′ = 6·77	5, 19 = 6·88	−0·11	0·03

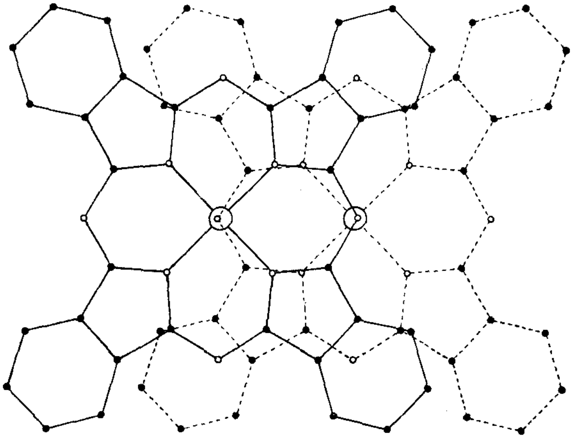
The differences are all less in nickel phthalocyanine, except the last two, which have changed in sign. The molecule has thus become more truly tetragonal with the insertion of the nickel atom, a fact which lends some support to the theory of internal hydrogen bonds previously discussed. But the remaining distortions are hard to explain. The molecule appears to retain a slight deformation of the same type as found in the free compound.

With regard to the minimum intermolecular distances and the arrangement of molecules in the crystal, the calculations and diagrams given for free phthalocyanine (*loc. cit.*, p. 1207) apply to the nickel derivative with sufficient accuracy for most purposes. The perpendicular

distance between the planes of parallel molecules situated at either end of the *b* axis translation is 3·38 A., and the normal projection of one of these molecules in the plane of the other is shown in Fig. 4. The dotted lines connect the atoms of one molecule whose plane lies 3·38 A. beneath the other. It is seen that the outer nitrogen atom of one molecule comes almost exactly over the nickel atom of the other molecule. The distance between the two atoms is thus only 3·38 A., which is practically equal to the closest distance of inter-molecular approach in the whole structure (compare data for free phthalocyanine).

In the crystal, therefore, the nickel atom is surrounded by six nitrogen atoms. Four of these lie at the corners of a square, 1·83 A. from the nickel atom, and bound to it by covalent (or co-ordinate) links. The other two lie vertically above and below the nickel atom, at a distance of 3·38 A. It can be seen from Fig. 4 that none of the other atoms in the molecule

FIG. 4.
Normal projection of two parallel molecules.



comes exactly over another in this manner. In fact, there is a distinct tendency for the atoms of the underlying molecule to be found in the gaps between the atoms of the upper molecule, a fact which probably governs the orientation assumed by the molecules in the crystal.

EXPERIMENTAL.

Fourier Analysis and Orientation of the Molecule.—The measurement of intensities and examples of the determination of phase constants for nickel phthalocyanine have already been described (*loc. cit.*, p. 1196). In preparing the contour map shown in Fig. 1, the electron-density series for the ($h0l$) zone was summed at 1800 different points on the asymmetric unit, the axial sub-divisions being the same as those employed for free phthalocyanine. Measurements from the map are referred to the molecular axes L and M (Fig. 2). The 19 lines connecting pairs of atoms in the L direction, (7, 7′), (8, 14), (9, 13), etc., are all found to be parallel to within $\pm$ 0·5°, and their mean direction makes an angle of 69·45° with the a axis (η_L). Similarly, the 19 lines connecting atoms in the M direction, (11, 11′), (10, 12′), (9, 13′), etc., are parallel to within $\pm$ 0·35°, and their mean direction makes an angle of $-$ 22·4° with the a axis (η_M). For free phthalocyanine we found $\eta_L = 69·3°$ and $\eta_M = -22·9°$. The difference of 0·5° in η_M is probably significant, as we should estimate the error in the mean value for the 19 lines at 0·1° to 0·2°.

The inclination of the M molecular axis to the b axis of the crystal (ψ_M) can be calculated in the manner previously described, by making use of the four benzene rings as "indicators." The results are as follows :

Ring 1 . . . 4, $\psi_M = 46{\cdot}6°$. Ring 15 . . . 18, $\psi_M = 45{\cdot}2°$.
Ring 1′ . . . 4′, $\psi_M = 45{\cdot}9°$. Ring 15′ . . . 18′, $\psi_M = 45{\cdot}8°$.
Mean $\psi_M = 45{\cdot}9°$.

The mean result is probably accurate to within 1°, and it happens to be identical with ψ_M for free phthalocyanine. From these figures, and the six equations given in the previous paper, the complete orientation of the molecule in the crystal can be calculated, with the following results :

$\chi_L = 69{\cdot}5°$ cos $\chi_L = 0{\cdot}3508$ $\chi_M = 48{\cdot}4°$ cos $\chi_M = 0{\cdot}6638$
$\psi_L = 88{\cdot}1°$ cos $\psi_L = 0{\cdot}0335$ $\psi_M = 45{\cdot}9°$ cos $\psi_M = 0{\cdot}6960$
$\omega_L = 20{\cdot}6°$ cos $\omega_L = 0{\cdot}9358$ $\omega_M = 105{\cdot}9°$ cos $\omega_M = -0{\cdot}2737$

$\chi_N = 131{\cdot}3°$ cos $\chi_N = -0{\cdot}6605$
$\psi_N = 44{\cdot}2°$ cos $\psi_N = 0{\cdot}7173$
$\omega_N = 77{\cdot}2°$ cos $\omega_N = 0{\cdot}2223$

Molecular Dimensions and Co-ordinates.—The positions of the atoms obtained by measurement of the contour map are given in Table III. Individual measurements of the co-ordinates taken parallel to the L and the M axis are first given (l and m) and in the last two columns the mean value is multiplied by the sine of the inclination of the molecular axis to the b crystal axis, along which the projection is made. This gives the actual molecular co-ordinates, L and M, from which the dimensions and angles in Fig. 2 are calculated. The accuracy varies somewhat in different parts of the projection; *e.g.*, the M co-ordinates of atoms 9 and 10 are less certain than their L co-ordinates. But in general the error should not be greater than 0·02—0·04 A.

TABLE III.

Co-ordinates with Respect to Molecular Axes.

			Mean value, A.	
Atoms.	l measured, A.	m measured, A.	$L(l \sin \psi_L)$.	$M(m \sin \psi_M)$.
1, 15	5·12, 5·11	2·98, 3·02	±5·11	4·18
2, 16	4·11, 4·08	3·70, 3·70	±4·09	5·15
3, 17	2·78, 2·74	3·42, 3·38	±2·76	$4{\cdot}73_5$
4, 18	2·45, 2·42	2·45, 2·41	$\pm 2{\cdot}43_5$	$3{\cdot}38_5$
5, 19	3·45, 3·43	1·75, 1·75	±3·44	2·44
6, 20	4·78, 4·78	2·02, 2·05	±4·78	2·83
7	3·42	0	±3·42	0
8, 14	2·69, 2·69	0·85, 0·83	±2·69	1·17
9, 13	1·31, 1·29	0·92, 0·92	±1·30	1·28
10, 12	1·18, 1·18	1·91, 1·91	±1·18	2·66
11	0	$2{\cdot}41_5$	0	3·36

The co-ordinates of the atoms referred to the monoclinic crystal axes can be obtained by combining the molecular co-ordinates with the orientation direction cosines given above, or by direct measurement from the Fourier projection. The results are given in Table IV, and these values are used in the structure factor calculations.

Calculation of Structure Factors. Electron Counts.—From the crystal co-ordinates of free phthalocyanine (J., 1936, 1204) and the formulæ for the space group $P2_1/a$ (cf. "International Tables for the Determination of Crystal Structure," Vol. I, p. 102) the geometrical structure factors of all the reflections of free phthalocyanine have been calculated. The signs of the factors so obtained are found to agree in every case with the direct experimental determinations of the phase constants upon which this analysis has been based, except for the very weak (16, 0, 1) which has changed from − to +. This single change can have no significant effect on the projection.

The proper structure factors, F, which express the ratio of the amplitude actually given by a reflection to the amplitude which would be given if the contents of the unit cell were replaced by a single electron, were obtained from the relation $F = Sf$, where S is the geometrical structure factor, and f is a function which expresses the average reflecting power of the atoms in the crystal, in terms of θ, the angle of incidence of the rays. As 64 out of the 80 atoms (without counting hydrogen) in the unit cell of phthalocyanine are carbon, we have employed the f-values for typical organic hydrocarbons (*Proc. Roy. Soc.*, *A*, 1935, **150**, 110), increasing the contributions

TABLE IV.

Co-ordinates with Respect to Monoclinic Crystal Axes. Centre of Symmetry as Origin.

Atom.	x, A.	$2\pi x/a$.	y, A.	$2\pi y/b$.	z, A.	$2\pi z/c$.
Ni	0	0°	0	0°	0	0°
1 CH	6·83	123·6	3·08	235·3	4·29	103·6
2 CH	6·36	115·0	3·72	284·4	2·85	68·9
3 CH	4·91	88·9	3·39	258·9	1·51	36·6
4 C	3·94	71·3	2·44	186·2	1·59	38·5
5 C	4·41	79·8	1·81	138·5	3·01	72·7
6 CH	5·86	105·9	2·13	162·9	4·36	105·3
7 N	3·19	57·7	0·12	8·8	3·77	91·1
8 C	3·09	55·9	0·90	69·1	2·59	62·6
9 N	1·85	33·4	0·94	71·6	1·02	24·6
10 C	2·41	43·7	1·89	144·5	0·44	10·7
11 N	1·66	30·0	2·34	178·8	−1·08	− 26·2
12 C	0·21	3·8	1·81	138·5	−2·16	− 52·2
13 N	−0·58	−10·5	0·85	64·8	−1·85	− 44·6
14 C	−1·93	−35·0	0·72	55·3	−3·34	− 80·8
15 CH	−2·71	−49·0	2·74	209·1	−6·98	−168·7
16 CH	−1·28	−23·1	3·45	263·5	−6·17	−149·1
17 CH	−0·24	− 4·3	3·20	244·8	−4·57	−110·4
18 C	−0·60	−10·9	2·27	173·8	−3·78	− 91·2
19 C	−2·01	−36·3	1·58	120·9	−4·58	−110·6
20 CH	−3·07	−55·4	1·81	138·5	−6·18	−149·4

of the nitrogen atoms relative to the carbon atoms by 20%, which is rather more than the ratio suggested by their atomic numbers.

The F values calculated in this manner are considerably below the measured values, and they require to be increased by a constant factor of 1·33 in order to afford the best agreements. Owing to the small size of the crystals upon which the absolute measurements were based (0·040—0·068 mg.) the *scale* of the measured F values may be in error by 5% or even more, but it does not seem possible to explain the factor 1·33 in this manner. The high measured F values are most likely due to the temperature factor for phthalocyanine (which takes account of the thermal movement of the atoms) being much less than in the case of typical organic hydrocarbons. This explanation is very probable in view of the high m. p. of the compound (> 500°). We have made no attempt to correct for the temperature effect in detail, but all the calculated values of F have been increased by the correlating factor of 1·33.

The measured and calculated values of F for free phthalocyanine are given in cols. 3 and 4 of Table V. In col. 5, the contributions to the structure factors of the two nickel atoms are given. These values are taken from Brindley's experimentally determined scattering curve (*Phil. Mag.*, **1936**, **21**, 778), but for the $(h + k)$ odd reflections the contributions from the two nickel atoms are in opposite phase and the resultant is zero.

In the last two columns of the table the measured and calculated values of F for nickel phthalocyanine are given. The calculated values are derived from those of free phthalocyanine by the algebraic addition of the contributions from the nickel atoms. This method is sufficiently accurate to test the general agreements and the signs used in the Fourier analysis, which are all found to be correct for nickel phthalocyanine.

It is possible to make a more accurate calculation of the structure factors for nickel phthalocyanine by means of the revised co-ordinates given in Table IV of this paper; but as the displacement of the atoms, compared with free phthalocyanine, is small, differences will only be found in the higher-order reflections. A number of these structure factors with high indices have been recalculated in this manner, and it is found that on the average a small improvement in the agreements is obtained, particularly for the (16, 0, 1) and (16, 0, 2) planes. It would seem, however, that the estimated contributions of the nickel atoms (from Brindley's curve) are considerably too great for the furthest out reflections of large glancing angle (θ).

The general order of agreement between measured and calculated values of F is quite equal to that obtained for other more simple structures which have been successfully analysed. This is shown by the following figures which give the sum of the discrepancies between the measured and calculated values, expressed as a percentage of the total measured F values, for different zones in the two compounds. Absent reflections are included.

	$(0kl)$ Zone.	$(h0l)$ Zone.	$(hk0)$ Zone.	All reflections.
Free phthalocyanine	11·1	13·2	13·8	12·5
Ni phthalocyanine	14·0	14·4	15·1	14·2

TABLE V.

Measured and Calculated Values of the Structure Factor.

	sin θ	$(C_{32}H_{16}N_8)H_2$.			$C_{32}H_{16}N_8Ni$.	
hkl.	(λ = 1·54).	*F*, meas.	*F*, calc.	Ni 2*F*.	*F*, meas.	*F*, calc.
200	0·092	< 5	+ 15	52	55	+ 67
400	0·183	46	− 48	47	< 6	− 1
600	0·275	38	+ 33	40	80	+ 73
800	0·367	< 9	+ 12	33	44	+ 45
10,00	0·458	11	+ 10	28	44	+ 38
12,00	0·550	16	+ 23	24	41	+ 47
14,00	0·641	<12	− 5	21	14	+ 16
16,00	0·733	15	− 21	17	<15	− 4
020	0·326	9	− 12	36	21	+ 24
040	0·652	6	+ 4	20	22	+ 24
001	0·062	78	+ 95	54	112	+149
002	0·123	85	− 95	51	37	− 44
003	0·184	39	− 41	46	10	+ 5
004	0·246	17	+ 11	42	56	+ 53
005	0·307	60	− 53	37	13	− 16
006	0·369	50	− 44	33	18	− 11
007	0·430	24	+ 25	30	57	+ 55
008	0·491	28	− 27	26	<11	− 1
009	0·553	10	− 7	24	18	+ 17
00,10	0·614	13	+ 21	22	34	+ 43
00,11	0·676	<12	+ 1	19	16	+ 20
00,12	0·737	<15	+ 6	17	<15	+ 23
011	0·174	36	− 39	0	33	− 39
012	0·204	36	− 36	0	35	− 36
013	0·246	<11	+ 16	0	<11	+ 16
014	0·295	<12	+ 1	0	<12	+ 1
015	0·348	35	+ 28	0	35	+ 28
016	0·403	38	+ 32	0	41	+ 32
017	0·460	23	+ 29	0	31	+ 29
018	0·516	<19	− 1	0	<19	− 1
019	0·576	<20	− 9	0	<20	− 9
01,10	0·636	<21	− 12	0	<21	− 12
021	0·332	<13	− 3	36	39	+ 33
022	0·349	<13	0	35	37	+ 35
023	0·375	15	+ 15	33	47	+ 48
024	0·408	48	+ 43	31	74	+ 74
025	0·448	16	− 16	29	18	+ 13
026	0·492	22	− 24	26	<16	+ 2
027	0·540	<18	− 7	24	27	+ 17
028	0·580	24	+ 27	23	59	+ 50
029	0·642	<21	− 5	21	18	+ 16
031	0·493	<17	+ 3	0	<17	+ 3
032	0·504	<17	+ 8	0	<17	+ 8
033	0·522	16	− 19	0	14	− 19
034	0·547	<17	+ 3	0	<17	+ 3
035	0·577	<17	+ 4	0	<17	+ 4
036	0·612	<17	0	0	<17	0
037	0·651	<17	+ 13	0	<17	+ 13
041	0·655	<17	+ 9	20	31	+ 29
042	0·663	<17	+ 3	20	19	+ 23
043	0·677	<20	+ 3	19	<20	+ 22
20,11	0·729	19	− 21	17	<15	− 4
20,10	0·668	43	− 43	20	20	− 23

	sin θ	$(C_{32}H_{16}N_8)H_2$.			$C_{32}H_{16}N_8Ni$.	
hkl.	(λ = 1·54).	*F*, meas.	*F*, calc.	Ni 2*F*.	*F*, meas.	*F*, calc.
209	0·606	14	− 9	22	<12	+ 13
208	0·546	15	+ 13	24	39	+ 37
207	0·485	24	+ 20	27	51	+ 47
206	0·425	<10	+ 4	30	26	+ 34
205	0·364	72	− 54	34	29	− 20
204	0·305	10	+ 15	38	55	+ 53
203	0·246	13	− 16	42	31	+ 26
202	0·189	6	+ 21	46	54	+ 67
201	0·135	92	−116	50	43	− 66
$20\bar{1}$	0·079	96	+107	53	137	+160
$20\bar{2}$	0·107	17	+ 28	52	71	+ 80
$20\bar{3}$	0·156	67	+ 59	49	113	+108
$20\bar{4}$	0·212	61	− 55	44	11	− 11
$20\bar{5}$	0·270	36	+ 27	40	74	+ 67
$20\bar{6}$	0·329	< 9	+ 11	36	38	+ 47
$20\bar{7}$	0·389	21	+ 17	32	50	+ 49
$20\bar{8}$	0·449	<11	+ 9	29	41	+ 38
$20\bar{9}$	0·510	<11	+ 11	26	28	+ 37
$20,\bar{10}$	0·571	<12	− 10	23	17	+ 13
$20,\bar{11}$	0·632	38	− 37	21	11	− 16
$20,\bar{12}$	0·693	<12	+ 1	19	<12	+ 20
$20,\bar{13}$	0·757	38	+ 39	17	41	+ 56
40,10	0·729	<15	− 5	17	<15	+ 12
409	0·669	<12	+ 15	20	27	+ 35
408	0·609	<12	− 2	22	21	+ 20
407	0·550	10	+ 5	24	35	+ 29
406	0·491	35	+ 27	26	58	+ 53
405	0·434	13	− 17	29	<11	+ 12
404	0·377	66	− 61	33	28	− 28
403	0·322	< 9	+ 12	36	46	+ 48
402	0·270	< 7	+ 1	40	50	+ 41
401	0·222	12	− 16	44	29	+ 28
$40\bar{1}$	0·159	78	+ 75	48	129	+123
$40\bar{2}$	0·157	85	− 96	48	46	− 48
$40\bar{3}$	0·178	74	− 83	47	30	− 36
$40\bar{4}$	0·214	48	− 46	44	< 6	− 2
$40\bar{5}$	0·261	37	− 24	41	< 7	+ 17
$40\bar{6}$	0·312	< 8	− 5	37	33	+ 32
$40\bar{7}$	0·367	42	+ 35	33	73	+ 68
$40\bar{8}$	0·423	59	+ 58	30	91	+ 88
$40\bar{9}$	0·481	13	+ 11	27	35	+ 38
$40,\bar{10}$	0·539	16	+ 15	25	38	+ 40
$40,\bar{11}$	0·599	<12	+ 5	22	27	+ 27
$40,\bar{12}$	0·658	24	− 21	20	<12	− 1
$40,\bar{13}$	0·716	16	− 21	18	<15	− 3
609	0·737	<15	− 11	17	<15	+ 6
608	0·679	16	+ 15	19	33	+ 34
607	0·622	56	+ 53	21	78	+ 74
606	0·565	32	+ 34	23	50	+ 57
605	0·510	29	+ 21	26	49	+ 47
604	0·456	26	+ 16	28	43	+ 44
603	0·405	33	− 23	31	<10	+ 8
602	0·356	75	− 66	34	40	− 32
601	0·312	37	− 30	37	< 8	+ 7
$60\bar{1}$	0·298	40	− 40	38	< 7	− 2

TABLE V (*continued*).

hkl.	sin θ (λ = 1·54).	$(C_{32}H_{16}N_8)H_2$. F, meas.	$(C_{32}H_{16}N_8)H_2$. F, calc.	Ni 2F.	$C_{32}H_{16}N_8Ni$. F, meas.	$C_{32}H_{16}N_8Ni$. F, calc.
$60\bar{2}$	0·234	55	− 53	43	11	− 10
$60\bar{3}$	0·236	31	− 33	43	10	+ 10
$60\bar{4}$	0·253	< 7	+ 7	41	44	+ 48
$60\bar{5}$	0·283	16	− 21	39	25	+ 18
$60\bar{6}$	0·322	31	+ 32	36	66	+ 68
$60\bar{7}$	0·367	30	+ 18	33	56	+ 51
$60\bar{8}$	0·416	17	+ 13	30	44	+ 43
$60\bar{9}$	0·468	22	− 27	28	<11	+ 1
$60,\bar{1}\bar{0}$	0·522	<12	+ 2	25	26	+ 27
$60,\bar{1}\bar{1}$	0·578	<12	− 2	23	26	+ 21
$60,\bar{1}\bar{2}$	0·635	<12	+ 6	21	22	+ 27
$60,\bar{1}\bar{3}$	0·692	24	− 18	19	<12	+ 1
$60,\bar{1}\bar{4}$	0·750	27	− 22	17	<15	− 5
808	0·754	<14	− 5	17	<14	+ 12
807	0·698	<12	+ 7	19	26	+ 26
806	0·644	26	+ 30	20	42	+ 50
805	0·591	<12	− 13	23	<12	+ 10
804	0·539	19	+ 15	25	41	+ 40
803	0·490	<11	+ 3	27	29	+ 30
802	0·444	22	+ 25	29	50	+ 54
801	0·403	<10	− 4	31	31	+ 27
$80\bar{1}$	0·338	20	+ 17	35	59	+ 52
$80\bar{2}$	0·318	< 8	− 3	37	30	+ 34
$80\bar{3}$	0·310	15	+ 13	37	55	+ 50
$80\bar{4}$	0·314	9	− 7	37	38	+ 30
$80\bar{5}$	0·330	13	− 11	36	22	+ 25
$80\bar{6}$	0·355	< 9	+ 3	34	42	+ 37
$80\bar{7}$	0·389	14	− 15	32	16	+ 17
$80\bar{8}$	0·427	42	+ 43	30	67	+ 73
$80\bar{9}$	0·473	44	+ 41	27	66	+ 68
$80,\bar{1}\bar{0}$	0·521	15	− 19	25	<12	+ 6
$80,\bar{1}\bar{1}$	0·572	38	− 41	23	14	− 18
$80,\bar{1}\bar{2}$	0·624	<12	− 11	21	<12	+ 10
$80,\bar{1}\bar{3}$	0·678	27	+ 32	19	46	+ 51
$80,\bar{1}\bar{4}$	0·733	18	− 19	17	<15	− 2
10,07	0·775	12	− 20	16	<14	− 4
10,06	0·725	<15	+ 1	18	16	+ 19
10,05	0·674	17	− 15	19	<12	+ 4
10,04	0·625	19	− 11	21	<12	+ 10
10,03	0·578	13	+ 18	23	36	+ 41
10,02	0·534	25	− 29	25	<12	− 4
10,01	0·494	<11	+ 2	26	26	+ 28
$10,0\bar{1}$	0·429	62	+ 60	30	94	+ 90
$10,0\bar{2}$	0·406	20	+ 19	31	51	+ 50
$10,0\bar{3}$	0·392	28	+ 20	32	61	+ 52
$10,0\bar{4}$	0·388	13	+ 16	32	44	+ 48
$10,0\bar{5}$	0·393	13	− 19	32	17	+ 13
$10,0\bar{6}$	0·407	27	+ 22	31	59	+ 53
$10,0\bar{7}$	0·430	<10	+ 4	30	31	+ 34
$10,0\bar{8}$	0·460	46	− 46	28	17	− 18
$10,0\bar{9}$	0·495	15	+ 11	26	41	+ 37
$10,0,\bar{1}\bar{0}$	0·536	<12	+ 6	25	33	+ 31
$10,0,\bar{1}\bar{1}$	0·580	<12	+ 12	23	31	+ 35
$10,0,\bar{1}\bar{2}$	0·627	12	− 13	21	<12	+ 8
$10,0,\bar{1}\bar{3}$	0·676	25	+ 26	19	38	+ 45
$10,0,\bar{1}\bar{4}$	0·727	<15	+ 9	18	24	+ 27
12 05	0·759	<14	− 6	16	<14	+ 10
12,04	0·711	35	− 42	18	16	− 24
12,03	0·666	<12	− 6	20	21	+ 14
12,02	0·624	11	− 11	21	<12	+ 10
12,01	0·585	<12	− 6	23	22	+ 17
$12,0\bar{1}$	0·519	12	+ 13	25	38	+ 38
$12,0\bar{2}$	0·495	<11	− 5	26	22	+ 21
$12,0\bar{3}$	0·478	13	− 18	27	15	+ 9
$12,0\bar{4}$	0·467	52	+ 60	28	81	+ 88
$12,0\bar{5}$	0·465	11	+ 6	28	29	+ 34
$12,0\bar{6}$	0·471	41	− 43	27	21	− 16
$12,0\bar{7}$	0·485	31	− 27	27	<11	0
$12,0\bar{8}$	0·505	42	− 38	26	13	− 12
$12,0\bar{9}$	0·532	13	− 7	25	<12	+ 18
$12,0,\bar{1}\bar{0}$	0·565	10	+ 16	23	38	+ 39
$12,0,\bar{1}\bar{1}$	0·602	<12	+ 11	22	26	+ 33
$12,0,\bar{1}\bar{2}$	0·643	9	+ 12	21	33	+ 33
$12,0,\bar{1}\bar{3}$	0·686	<12	+ 3	19	18	+ 22
$12,0,\bar{1}\bar{4}$	0·732	21	+ 27	17	36	+ 44
14,03	0·756	<14	+ 13	17	18	+ 30
14,02	0·714	14	+ 16	18	18	+ 34
14,01	0·676	33	− 37	19	15	− 18
$14,0\bar{1}$	0·611	<12	− 1	22	25	+ 21
$14,0\bar{2}$	0·585	<12	+ 3	23	25	+ 26
$14,0\bar{3}$	0·565	29	− 28	23	<12	− 5
$14,0\bar{4}$	0·551	10	− 11	24	15	+ 13
$14,0\bar{5}$	0·543	11	+ 11	24	35	+ 35
$14,0\bar{6}$	0·543	16	+ 11	24	40	+ 35
$14,0\bar{7}$	0·549	9	+ 11	24	33	+ 35
$14,0\bar{8}$	0·562	22	− 20	24	<12	+ 4
$14,0\bar{9}$	0·582	37	− 35	23	10	− 12
$14,0,\bar{1}\bar{0}$	0·606	<12	+ 7	22	24	+ 29
$14,0,\bar{1}\bar{1}$	0·637	<12	− 9	21	<12	+ 12
$14,0,\bar{1}\bar{2}$	0·671	<12	− 1	20	<12	+ 19
$14,0,\bar{1}\bar{3}$	0·709	<16	+ 5	18	16	+ 23
$14,0,\bar{1}\bar{4}$	0·749	<15	+ 9	17	13	+ 26
16,02	0·805	16	+ 25	15	24	+ 40
16,01	0·767	10	+ 10	16	<14	+ 26
$16,0\bar{1}$	0·702	13	− 11	18	<16	+ 7
$16,0\bar{2}$	0·675	10	+ 15	19	29	+ 34
$16,0\bar{3}$	0·653	<12	+ 7	20	17	+ 27
$16,0\bar{4}$	0·637	29	− 31	21	<12	− 10
$16,0\bar{5}$	0·625	<12	− 2	21	17	+ 19
$16,0\bar{6}$	0·620	<12	+ 10	21	31	+ 31
$16,0\bar{7}$	0·621	<12	+ 7	21	26	+ 28
$16,0\bar{8}$	0·628	<12	− 6	21	10	+ 15
$16,0\bar{9}$	0·641	9	+ 10	21	33	+ 31
$16,0,\bar{1}\bar{0}$	0·659	10	+ 7	20	30	+ 27
$16,0,\bar{1}\bar{1}$	0·682	10	+ 11	19	32	+ 30
$16,0,\bar{1}\bar{2}$	0·710	<16	+ 4	18	15	+ 22
$16,0,\bar{1}\bar{3}$	0·741	<15	+ 5	17	12	+ 22
$18,0\bar{2}$	0·766	27	− 31	16	<14	− 15
$18,0\bar{3}$	0·742	<15	+ 1	17	12	+ 18
$18,0\bar{4}$	0·724	26	+ 27	18	38	+ 45
$18,0\bar{5}$	0·710	27	+ 29	18	36	+ 47
$18,0\bar{6}$	0·702	<16	+ 1	18	14	+ 19
$18,0\bar{7}$	0·697	<16	+ 11	19	27	+ 30
$18,0\bar{8}$	0·699	<16	+ 2	19	11	+ 21

TABLE V (*continued*).

hkl.	sin θ (λ = 1·54).	$(C_{32}H_{16}N_8)H_2$. *F*, meas.	$(C_{32}H_{16}N_8)H_2$. *F*, calc.	Ni 2*F*.	$C_{32}H_{16}N_8Ni$. *F*, meas.	$C_{32}H_{16}N_8Ni$. *F*, calc.	*hkl.*	sin θ (λ = 1·54).	$(C_{32}H_{16}N_8)H_2$. *F*, meas.	$(C_{32}H_{16}N_8)H_2$. *F*, calc.	Ni 2*F*.	$C_{32}H_{16}N_8Ni$. *F*, meas.	$C_{32}H_{16}N_8Ni$. *F*, calc.
18,0$\bar{9}$	0·706	<16	− 5	18	<16	+ 13	520	0·399	32	− 37	0	26	− 37
18,0,$\bar{1}\bar{0}$	0·718	<15	+ 5	18	16	+ 23	620	0·427	14	+ 17	30	52	+ 47
18,0,$\bar{1}\bar{1}$	0·736	<15	+ 8	17	16	+ 25	720	0·457	<10	0	0	<16	0
20,0$\bar{6}$	0·785	<14	+ 12	16	12	+ 28	820	0·491	10	− 15	26	<16	+ 11
20,0$\bar{7}$	0·778	<14	+ 9	16	<14	+ 25	920	0·526	<11	− 5	0	<18	− 5
20,0$\bar{8}$	0·775	<14	− 1	16	<14	+ 15	10,20	0·562	<11	+ 9	24	15	+ 33
20,0$\bar{9}$	0·777	14	− 18	16	13	− 2	11,20	0·600	36	− 33	0	24	− 33
20,0,$\bar{1}\bar{0}$	0·785	<14	+ 15	16	12	+ 31	12,20	0·639	12	− 17	21	<19	+ 4
							13,20	0·679	<14	+ 7	0	<23	+ 7
110	0·169	66	− 71	48	9	− 23	14,20	0·719	17	+ 13	18	<23	+ 31
210	0·187	53	+ 63	0	44	+ 63	130	0·491	14	− 12	26	<18	+ 14
310	0·213	19	− 19	44	20	+ 25	230	0·497	<11	− 8	0	<18	− 8
410	0·245	21	− 23	0	14	− 23	330	0·508	<11	− 4	26	13	+ 22
510	0·281	< 7	− 4	39	38	+ 35	430	0·522	<11	− 1	0	<18	− 1
610	0·320	10	− 4	0	<11	− 4	530	0·540	13	+ 20	24	31	+ 44
710	0·360	< 8	+ 1	34	37	+ 35	630	0·561	<11	− 11	0	<19	− 11
810	0·401	12	+ 16	0	<14	+ 16	730	0·585	<12	+ 7	23	21	+ 30
910	0·443	28	− 25	29	<15	+ 4	830	0·611	<13	+ 5	0	<21	+ 5
10,10	0·486	16	− 12	0	<16	− 12	930	0·640	<14	+ 8	21	<23	+ 29
11,10	0·529	<11	+ 3	25	29	+ 28	10,30	0·670	22	+ 20	0	<23	+ 20
12,10	0·573	<11	− 11	0	<19	− 11	11,30	0·702	<14	+ 4	18	<23	+ 22
13,10	0·618	<13	0	22	<21	+ 22	140	0·653	11	− 12	0	<20	− 12
14,10	0·661	<14	+ 9	0	<23	+ 9	240	0·659	<12	− 4	20	<20	+ 16
15,10	0·706	<14	− 12	18	<23	+ 6	340	0·666	<12	− 1	0	<20	− 1
120	0·329	< 7	− 5	0	<13	− 5	440	0·677	<14	+ 9	19	<23	+ 28
220	0·339	11	− 19	35	13	+ 16	540	0·691	<14	+ 11	0	<23	+ 11
320	0·354	< 8	− 7	0	<13	− 7	640	0·707	<14	− 9	18	<23	+ 9
420	0·374	< 8	− 1	33	23	+ 32	740	0·726	16	+ 24	0	<23	+ 24

The measured structure factors of the two strongest reflections for nickel phthalocyanine, the (001) and (20$\bar{1}$), are considerably less than the calculated values, probably owing to an extinction effect for which we have not been able to correct. This deficiency is shown in another way when an electron count is made for the nickel atom. When the density is integrated over the area of the nickel atom, we find 25·6 electrons instead of 28 as required by the atomic number of nickel. But if the amplitudes of the component terms in the Fourier series due to the (001) and (20$\bar{1}$) reflections are increased to the calculated values, the electron count gives a result of 26·9. The remaining deficiency of one electron is probably due to the omission of weak reflections lying beyond our experimental limits, the majority of which will make positive contributions, and so add to the density on the nickel atom.

An electron count has also been carried out on the nitrogen atom 11, which is one of the best resolved atoms in the structure, and sufficiently clear of its neighbours to give accurate results. The value obtained is 7·0 electrons.

SUMMARY.

The structure of nickel phthalocyanine has been determined by a double Fourier synthesis of the X-ray crystal data for the (*h*0*l*) zone of reflections, employing absolute measurements of intensities and a direct determination of the phase constants by comparisons with free phthalocyanine. The results are expressed by a contoured electron-density map of the molecule in which every atom is separately resolved. The 60 parameters of the structure are determined to within 0·02—0·04 A. The molecule is planar, and its orientation in the crystal is practically identical with that of free phthalocyanine. The structure of the molecule is also closely similar to that of free phthalocyanine, but there is a definite inward shift, amounting to about 0·09 A., of each of the four *iso*indole nitrogen atoms towards the central nickel atom to which they are bound by covalent links. The C–N interatomic distance of the inner nucleus is 1·38 A., slightly greater than the value found for free

phthalocyanine. The molecule is more nearly tetragonal than free phthalocyanine, but a small deformation still exists.

The structures assigned to nickel phthalocyanine and free phthalocyanine have been verified by the calculation of all the structure factors from the co-ordinates of the atoms. Some electron counts are given.

In conclusion, we wish to thank Sir William Bragg and the Managers of the Royal Institution for their continued interest in this work.

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38. *Optically Active Alkylsuccinic Acids. Part I. Resolution of* r-*Ethylsuccinic Acid into its Optical Antipodes.*

By HENRY WREN and JOHN CRAWFORD.

FOR comparison with the optically active phenyl- and diphenyl-succinic acids (J., 1916, **109**, 572; 1915, **107**, 406) suitable alkyl- and dialkyl-succinic acids were required. Their low specific rotation renders the known, active methyl- and dimethyl-succinic acids inconvenient for this purpose. *r*-Ethylsuccinic acid has therefore been resolved into its optical antipodes.

The inactive acid is conveniently prepared by condensing ethyl cyanoacetate with ethyl α-bromobutyrate in presence of sodium ethoxide in ethyl alcohol to afford ethyl α-cyano-β-ethylsuccinate, b. p. 156°/10 mm., which is hydrolysed by boiling hydrobromic acid (48%).

r-Ethylsuccinic acid (26·95 g.) and quinine (59·9 g.) were dissolved in boiling alcohol (400 c.c.). The solution, on cooling, deposited 49·4 g. of crystals which were further purified by repeated crystallisation from alcohol. The course of the resolution was followed by observation of the specific rotation of the acids obtained from the successive filtrates, the following values of $[\alpha]_D$ in acetone being obtained: − 4·4° − 4·4°, − 1·8°, + 2·7°, + 7·7°, + 8·43°, +8·38°. The remaining crop (13·1 g.) on decomposition with hydrochloric acid and extraction with ether gave 3·8 g. of crude *d*-ethylsuccinic acid, m. p. 69—74°, $[\alpha]_D$ + 19·4°, in acetone. Repeated crystallisation of this product from benzene–light petroleum gave pure d-*ethylsuccinic acid*, m. p. 83·5—85°, $[\alpha]_D^{16·8°}$ + 20·65° in acetone ($l = 2$, $c = 3·7284$) (Found: C, 49·2; H, 6·9. $C_6H_{10}O_4$ requires C, 49·3; H, 6·9%).

The lævorotatory by-products from the resolution described above were converted into the brucine salts, which were crystallised repeatedly from absolute alcohol. The acid obtained from the filtrates had successively $[\alpha]_D$ + 2·85°, + 5·71°, + 4·3°, − 2·7°, − 5·6°, − 8·6° and − 13·4° in acetone. The residual crop yielded a crude *l*-acid with $[\alpha]_D$ − 20·9° in acetone. This, when crystallised repeatedly from benzene–light petroleum, yielded homogeneous l-*ethylsuccinic acid*, m. p. 83—85°, $[\alpha]_D^{23·8}$ − 20·80° in acetone ($l = 2$, $c = 4·5944$) (Found: C, 49·5; H, 6·8%).

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39. *Optically Active Alkylsuccinic Acids. Part II. The Stereochemical Configuration of the Symmetrical Diethylsuccinic Acids.*

By HENRY WREN and JOHN W. E. HALLER.

ALTHOUGH the symmetrical dialkylsuccinic acids have been frequently investigated, the stereochemical configuration has been elucidated only in the case of the dimethyl acids, of which the isomeride of lower melting point has been resolved into its optical antipodes by Werner and Basyrin (*Ber.*, 1913, **46**, 3229). In the case of the s-diethylsuccinic acids the preparation of the isomeride, m. p. 190—192°, by the reduction of xeronic (diethylmaleic) acid (Otto, *Annalen*, 1887, **239**, 279) indicates that it probably has the *meso*-configuration, but the significance of this observation appears to have been overlooked by subsequent workers, most of whom have believed that the isomeride of lower melting point is the *meso*-

form as with the tartaric acids. Recent determinations of the heats of combustion of the dimethyl-, diethyl-, and diphenyl-succinic acids and their derivatives (Verkade and Hartman, *Rec. trav. chim.*, 1933, **52**, 9) show that if the diethylsuccinic acid, m. p. 130°, is regarded as the *r*-compound its properties resemble those of the proved *r*-dimethyl- and *r*-diphenyl-succinic acids (Wren and Still, J., 1915, **107**, 444) with respect to the mutual transformations of the *r*- and *meso*-acids and anhydrides, that in all cases the *r*-acid has the lower melting point, greater solubility in water at 25° and smaller energy content, but the values of the dissociation constants of the diethylsuccinic acids are oppositely situated to those of the corresponding dimethyl- and diphenyl-succinic acids.

The resolution of the *s*-diethylsuccinic acids has been examined in considerable detail by Bischoff (*Ber.*, 1891, **24**, 1068), who was unable to obtain evidence of activity by fractional crystallisation of the morphine salt of the acid, m. p. 190—192°, or by the action of *penicillium glaucum* on the acid. He found that the brucine, cinchonine, quinidine, morphine and strychnine salts of the acid, m. p. 130—132°, are not sufficiently crystalline for use in attempted resolutions, and that the acid is not attacked by *Penicillium glaucum*. He concluded that rotatory power depends on " the specific difference of the residues attached to the asymmetric carbon atom and that this difference is more marked when these groups are H, OH and CO_2H than when they are H, C_2H_5, CO_2H." On this account, therefore, he suggested that diethylsuccinic acid might be expected to have a lower rotatory power than tartaric acid, and that the difference in the solubilities of the alkaloidal salts of the two optically active isomerides would be less than in the case of the tartaric acids, so that separation of these salts by fractional crystallisation would be much more difficult, and perhaps impossible by known methods. The present experiences differ from those of Bischoff in that it has been found that the acid, m. p. 130—132°, under suitable conditions yields well-crystallised salts with brucine, cinchonine, morphine, cinchonidine, strychnine and, to a less extent, with quinine, and that resolution into its optical antipodes can be effected with brucine or cinchonine, although the process is more tedious than usual. It is thus established that the acid, m. p. 130—132°, is the racemic, and that of m. p. 190—192°, the *meso*-variety. In the cases of the dimethyl-, diethyl-, diphenyl-, and dibromo-succinic acids (McKenzie, J., 1911, **99**, 150; 1912, **101**, 1196; Holmberg, *Svensk Kem. Tidskr.*, 1911, No. 5; *J. pr. Chem.*, 1911, **84**, 145) the isomeride of lower m. p. is the racemic form, whereas the reverse is true with tartaric and dimethoxysuccinic acid.

The *s*-diethylsuccinic acids were first isolated by Hell (*Ber.*, 1873, **6**, 30) from the products of the action of methyl iodide and molecular silver on ethyl α-bromobutyrate, and subsequently obtained by Hell and Mühlhäuser (*Ber.*, 1880, **13**, 473) from silver and ethyl α-bromobutyrate only. Later, they were obtained by Bischoff and by Hjelt (*Ber.*, 1887, **20**, 2989, 3078; 1888, **21**, 2085, 2089) either from ethyl α-bromobutyrate and ethyl sodioethylmalonate or from the latter and ethyl chloromalonate; the recorded yields are only about 30% of the theoretical and the reactions are complicated by the production of glutaric derivatives (cf. von Auwers and Jackson, *Ber.*, 1890, **23**, 1599; Bone and Sprankling, J., 1899, **75**, 842). More satisfactory results in the preparation of certain alkyl-substituted succinic acids have been obtained by Bone and Sprankling (*loc. cit.*; J., 1900, **77**, 654, 1298) and by Bone, Sudborough, and Sprankling (J., 1904, **85**, 534) by replacing ethyl malonate and its homologues by ethyl cyanoacetate and its derivatives. This method has been extended by us to the *s*-diethylsuccinic acids by condensing ethyl cyanoacetate with sodium ethoxide and ethyl α-bromobutyrate to give ethyl α-cyano-β-ethylsuccinate, the sodium derivative of which is transformed by ethyl iodide into ethyl α-cyano-αβ-diethylsuccinate which is hydrolysed to the required acids. After the completion of this part of the work a similar method was described by Verkade and Hartman (*loc. cit.*), who, however, gave neither experimental details nor particulars of yield.

Preliminary trials were made, using ethyl acetoacetate. The condensation of ethyl sodioethylacetoacetate with ethyl α-bromobutyrate did not proceed very satisfactorily in ethyl alcohol, but the crude ethyl α-acetyl-αβ-diethylsuccinate gave when hydrolysed small amounts of the isomeric diethylsuccinic acids. Ethyl acetoacetate condensed readily with ethyl α-bromobutyrate, giving ethyl α-acetyl-β-ethylsuccinate, b. p. 157°/10 mm., in about 64% yield. This could not be ethylated by sodium and ethyl iodide in dry ether (cf.

Thompson, J., 1932, 2314), whereas in ethyl alcohol it afforded ethyl α-acetyl-αβ-diethylsuccinate, b. p. 167—169°/8 mm., in about 23% yield. This was treated catalytically with sodium ethoxide in ethyl alcohol (cf. von Miller, *Annalen*, 1880, **200**, 281; Dieckmann, *Ber.*, 1900, **33**, 261; Dieckmann and Kron, *Ber.*, 1908, **41**, 1266), giving ethyl acetate and ethyl diethylsuccinate, which was then hydrolysed by dilute alcoholic potash, but the results so obtained were less satisfactory than those given by direct hydrolysis with concentrated alcoholic potash. The over-all yields of the required acids were much lower than those obtained by the cyanoacetate method, so the work in this direction was not pursued further.

Experimental.

A solution of ethyl cyanoacetate (113 g.) in anhydrous alcohol (100 c.c.) was added slowly and with constant, vigorous shaking to a well-cooled solution of sodium (23 g.) in alcohol (320 c.c.), and ethyl α-bromobutyrate (200 g.) was slowly run in to the cold mixture. During the addition the temperature should not be allowed to rise. Subsequently the mixture was left with frequent shaking for about ½ hour, and then heated on the water-bath until a test portion was neutral to phenolphthalein. The alcohol was removed in a brine bath, the residue mixed with water, extracted with ether, the extract dried (calcium chloride), and the ether removed; on distillation, ethyl α-cyano-β-ethylsuccinate, b. p. 164°/21 mm., was obtained in 67% yield. A solution of this ester (100 g.) in alcohol (70 c.c.) was added slowly to sodium (10·13 g.) in alcohol (170 c.c.) and the product was treated gradually with ethyl iodide (69 g.); the mixture was heated on the water-bath until a test portion was neutral to phenolphthalein, after which excess of ethyl iodide and alcohol were removed by heating in a brine bath. The residue was diluted with ether, and the solution was thoroughly washed with water to remove a coloured impurity which otherwise passes into the finished product. The ethereal solution was further washed with concentrated brine, dried over calcium chloride and distilled, whereby ethyl α-cyano-αβ-diethylsuccinate, b. p. 167—170°/18 mm., was obtained in 79% yield, together with smaller amounts of more volatile material.

Hydrolysis and removal of the cyano-group from esters of this type proceeds with some difficulty. Bone and Sprankling (*loc. cit.*) in analogous cases recommend a two-stage process whereby the ester is first hydrolysed with alcoholic potash, and the cyano-acid is then treated with 50% sulphuric acid, whereas Verkade and Hartman (*loc. cit.*) use prolonged boiling with 20% hydrochloric acid, but do not give any particulars of yield. An almost quantitative hydrolysis can be obtained comparatively rapidly by the following procedure, which requires somewhat careful supervision, since too drastic treatment causes considerable carbonisation, whereas less rigorous conditions do not lead to complete hydrolysis. Concentrated sulphuric acid (24·4 c.c.) was added slowly and with vigorous shaking to the ester (30·1 g.) contained in a flask fitted with a ground-in air-condenser. Much heat was developed, and the flask was cooled somewhat after two-thirds of the acid had been added. The resultant yellow liquid was left for five minutes, after which water (6 c.c.) was slowly added and the flask was cautiously heated on a sand-bath. Brisk evolution of carbon dioxide occurred, and the temperature was slowly increased as the evolution of gas slackened. After ten minutes' heating, the flask was allowed to cool somewhat, and a further 6 c.c. of water were added dropwise and very cautiously through the air-condenser. When the vigorous ebullition caused by this addition had subsided, heating was continued for a further 15 minutes, after which 6 c.c. of water were added and boiling continued for a further 1½ hours. After addition of 25 c.c. of a mixture of concentrated sulphuric acid (25 c.c.) and water (20 c.c.), boiling was continued for two hours, after which the mixture was allowed to cool with frequent shaking. The crystals were removed on a sintered-glass filter, and washed repeatedly with small quantities of cold water. The combined filtrate and washings (about 200 c.c.) were boiled under a reflux condenser for 3 hours, thus giving a second crop which was removed and washed. The filtrate and washings were finally extracted with ether. The first two crops together weighed 18·1 g., and a further 2·4 g. were obtained from the ether. This last portion contained a very small amount of oily matter, which was readily removed by washing with a little cold benzene. The mixture of acids thus obtained was dissolved in boiling water; after decolorisation (animal charcoal), the solution deposited a crop of mixed acids, whilst further portions were obtained by concentration of the filtrate, and finally by extraction of it with ether. Treatment of the crops with boiling benzene left a residue of *meso*-diethylsuccinic acid, m. p. 190—192°, which is readily purified, if necessary, by crystallisation from water. The benzene solutions on cooling deposited *r*-diethylsuccinic acid, m. p. 130°. The final yields of homogeneous acids were 2·95 g. and 13·05 g. respectively.

Resolution of r-Diethylsuccinic Acid into its Optical Antipodes.—*r*-Diethylsuccinic acid (25 g.) and anhydrous brucine (113 g.) were dissolved in a hot mixture of rectified spirit (150 c.c.) and water (600 c.c.). On cooling, the solution readily deposited a well-crystallised crop (113·0 g.), which was purified by repeated crystallisation from 20% alcohol. The course of the resolution was followed by observation of the specific rotation of the acid recovered from the successive mother-liquors, the following values of $[\alpha]_{5461}$ in acetone being observed: − 22·6°, − 21·7°, − 14·8°, − 8·5°, − 2·3°, + 2·7°, + 10·4°, + 15·1°, + 23·8°, + 23·9°, + 27·8°, + 30·8°, and + 30·2°. The final crop of brucine salt (12·3 g.) gave 2·0 g. of the crude *d*-acid, with $[\alpha]_{5461}^{24°}$ + 32·8° in acetone (c = 5).

Crystallisation of it from boiling benzene yielded d-*diethylsuccinic acid*, m. p. 125°, $[\alpha]_{5461}^{24°}$ + 34·5°, or $[\alpha]_{\text{Hg yellow}}^{24°}$ + 30·9° in acetone; its specific rotation remained unchanged after further crystallisation [Found: 0·1004 g. of acid neutralised 22·87 c.c. of 0·05056*N*-$Ba(OH)_2$. $C_8H_{14}O_4$ requires 22·81 c.c.].

For the isolation of the pure *l*-acid the crude lævorotatory mixtures obtained in the above resolution were converted into the brucine salts, which were recrystallised from boiling 20% alcohol. The *l*-acid was thereby concentrated in the filtrate, from which it was removed and recombined with brucine, the process being continued until a sample with $[\alpha]_{5461}$ − 31·4° in acetone was obtained. Even when the mixture contains relatively little of the *d*-acid, crystallisation of the salts proceeds satisfactorily, although slowly. Recrystallisation of the sample from boiling benzene gave l-*diethylsuccinic acid*, m. p. 125°, $[\alpha]_{5461}^{25°}$ − 34·3°, $[\alpha]_{\text{Hg yellow}}^{25°}$ − 30·7° in acetone [Found: 0·1005 g. neutralised 23·00 c.c. of 0·05056*N*-$Ba(OH)_2$. $C_8H_{14}O_4$ requires 23·05 c.c.].

The solubility of the active acids is much greater than that of the *r*-acid, and it appears essential that the active material should have about $[\alpha]_{5461}$ ± 30° in acetone before the final purification from boiling benzene can be successfully accomplished. For instance, a sample, $[\alpha]_{5461}$ + 28·0° in acetone, when crystallised from benzene gave a product with $[\alpha]_{5461}$ + 26·8°, whereas that recovered from the mother-liquor had $[\alpha]_{5461}$ + 29·8°.

The resolution of *r*-diethylsuccinic acid by means of cinchonine in hot aqueous solution gave less satisfactory results. With molecular and half-molecular quantities of the alkaloid, the normal salt of the *d*-acid separated; crystallisation occurred less readily, and the resolution appeared to proceed more slowly than when brucine was employed.

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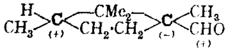
40. *The Rotatory Dispersion of Organic Compounds. Part XXX. Campholic Aldehyde.*

By (the late) T. M. LOWRY and W. C. G. BALDWIN.

MEASUREMENTS of the circular dichroism of camphor (Kuhn and Gore, *Z. physikal. Chem.*, 1931, *B*, **12**, 389) and of camphor-β-sulphonic acid (Lowry and French, J., 1932, 2654) have shown that the ultra-violet absorption band of the ketone is composite, since the optical activity is concentrated in the low-frequency half of the band. The maximum of circular dichroism is therefore displaced relatively to the maximum of absorption in the direction of *lower* frequencies from 2910 to 3020 A. in camphor, and from 2840 to 2900 A. in the sulphonic acid. Similarly in carvomenthone (Lowry and Lishmund, J., 1935, 709) the maximum of circular dichroism is displaced as in camphor by 110 A., from 2886 to 2995 A. The visual absorption band of camphorquinone (Part XXIX; J., 1936, 1156) is also composite, since the main optically active component is accompanied by two smaller inactive bands, one on either side of the principal band. On account of this symmetrical distribution of the components, the maximum of circular dichroism is slightly displaced in the direction of *higher* frequencies.

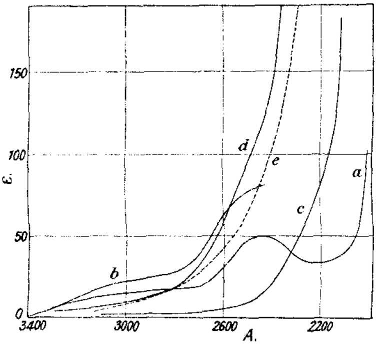
In the aldehydes, the evidence for complexity is much less clear than in the ketones. Thus, in a series of four open-chain aldehydic acetates (Part XXIII, J., 1933, 1179; Part XXV, J., 1935, 696) the maxima of absorption and of circular dichroism agreed within 10 A., the difference increasing to 30 A. only in the *ketonic* sugar, penta-acetyl μ-*d*-fructose; but

the composite character of the absorption is indicated (as in camphorquinone) by the greater half-width of the absorption band, as compared with the band of circular dichroism, in every case except penta-acetyl μ-*d*-glucose. In these circumstances, it was desirable to study the behaviour of a simple aldehyde, containing only hydrocarbon radicals in addition to the aldehydo-group, and this was made practicable by the generosity of Prof. H. Rupe of Basel, who prepared for us a specimen of campholic aldehyde (inset).



The results are of considerable interest, because the circular dichroism was found to have the normal frequency of an aldehydic band, although the absorption curve showed only a step-out at this wave-length. It also appeared that the principal optically active band at 2995 A. was accompanied by a secondary band of similar sign at about 3200 A. The constants of this secondary band of circular dichroism were therefore calculated from the

Fig. 1.



a. Absorption spectrum of campholic aldehyde in cyclo*hexane.*
b. ,, ,, ,, ,, chloroform.
c. ,, ,, ,, acid in alcohol.
d., *e.* *Absorption spectra of old* cyclo*hexane solutions of the aldehyde, after complete extraction of campholic acid.*

residual anomalies in the curve of rotatory dispersion. The subsidiary band discovered in other simple aldehydes by Schou (*Compt. rend.*, 1926, **182**, 965) also exists in campholic aldehyde, although completely hidden from view in a " step-out." It is also optically active, with the same sign as the main band, and in this respect differs from the aldehydic and ketonic sugars (*loc. cit.*).

Absorption.—A freshly prepared solution of the aldehyde in *cyclo*hexane showed (i) a step-out, passing through a point of inflexion $\varepsilon = 15$ at 2950 A., (ii) an absorption band with a maximum $\varepsilon = 50$ at 2450 A., and (iii) an intense general absorption beyond 2100 A. (Fig. 1*a*). A solution in chloroform gave a similar curve (Fig. 1*b*) but the absorption was about 50% greater, and the curve was cut off by the absorption of the chloroform before the maximum was reached. The absence of the usual aldehydic band was also proved by the use of a hydrogen discharge lamp as a source of continuous ultra-violet radiation.

A solution in *cyclo*hexane which had been kept for more than a year yielded a considerable extract of campholic acid, the absorption curve of which is shown in Fig. 1*c*; and when the whole of the acid had been extracted, it yielded a curve of general absorption, Fig. 1*d* or *e*, which we attribute to a condensation product of the aldehyde.

The absorption band at 2450 A. is abnormal in a simple aldehyde, since these usually exhibit a maximum at about 2900 A., but its origin is of no direct importance in the present research, since the circular dichroism is concentrated in the step-out, and there is no evidence that this band makes any substantial contribution to the rotatory power of the material. An analogy may be found in pulegone where the ketonic band at 2800 A. is replaced by a step-out (log ε = 1·625 at 3210 A.) and a band (log ε = 3·8 at 2430 A.), owing to conjugation, but curves (*c*), (*d*), and (*e*), which exhibit strong absorption only at wave-lengths less than 2450 A., lend little support to the view that the band is due either to oxidation or to condensation. Since no further material was available, we merely record the fact that a specimen of the aldehyde, which had been recently distilled in Basel into a glass tube and sealed up for transmission to Cambridge, gave the absorption curve shown in Fig. 1*a*, without prejudice to further enquiries as to the origin of the band.

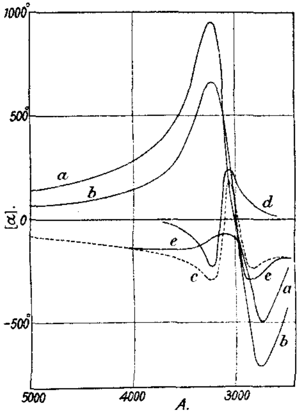
Circular Dichroism.—The circular dichroism reaches its maximum at 2995 A., with $(\varepsilon_l \sim \varepsilon_r)_{max.} = 0{\cdot}50$, and $\lambda' = 418$ A. The subsidiary band derived from the dispersion curve had the following parameters:

$\lambda_0 = 3140$ A., $(\varepsilon_l \sim \varepsilon_r)_{max.} = 0{\cdot}18$, $\lambda' = 160$ A.

Owing to the over-lapping of the two bands of similar sign, the curve is unusual in being steeper on the high-frequency side, but its components are more normal in shape.

The use of the subsidiary band gives a rotatory dispersion difference curve which is considerably nearer to the theoretical form, in that it does not cross the axis, behaviour which is quite impossible according to all theories for the analysis of dispersion from the activity of a simple band. There remains, however, in the final difference curve an anomaly which suggests the analysis to be not quite perfect. This is probably due to a second complicating subsidiary centred at 2940 A., since alteration of the primary –CHO contribution does little towards eliminating the anomaly. It should, however, also be mentioned that the extent of the maxima (Fig. 2*c*) is slightly exaggerated owing to the fact that the primary –CHO contribution should be calculated from the theoretical curve of simple circular dichroism. The difference, however, is slight, since the true extent of the subsidiary dispersion loop is about 170° as opposed to 240°, and the form remains unchanged.

FIG. 2.



a. *Observed rotations for campholic aldehyde.*
b. *Calculated carbonyl contribution.*
c. *Difference curve,* (a ~ b) *with sign reversed.*
d. *Calculated subsidiary component.*
e. *Final difference curve, showing third component.*

Rotatory Dispersion.—The rotatory dispersion was measured in two solvents, chloroform and *cyclo*hexane, in the regions of transparency and of absorption. The range of transparency high enough for Drude analyses was 6708—3768 A. with *cyclo*hexane as solvent, and 6708—3674 A. with chloroform. Three-constant, two-term equations were used to express the results, and the differences between the values for the two solvents were very slight. The value of λ_0 was in each case 2868 A. as compared with 2990 and 3000 A. from circular dichroism and absorption measurements respectively. The equations are of interest owing to their consisting of two terms of similar sign. This fact indicates directly that the predominant residual rotation as shown in Fig. 2 is not responsible for the induced activity of the aldehyde group, since these two terms could not under these conditions have the same sign. The results would indicate that the major part of the residual rotation is due to the asymmetric grouping in the γ position from the carbonyl group. The α asymmetric grouping is, however, responsible for the large induced dissymmetry, although the reason for the

complexity of the curve may be found in the independent interaction of the two centres with the carbonyl group. The analysis by Drude's equation thus leads to the same general results as that by the more complete method, and the signs of the partial rotations are indicated on the formula above. A comparison shows campholic aldehyde to be analogous to menthone and carvomenthone (*loc. cit.*) in this respect.

Rotatory Dispersion of Campholic Aldehyde in cyclo*Hexane at* 20°.

(a) c = 16·6525 g./100 c.c.; l = 2 dm. (b) c = 16·6127 g./100 c.c.; l = 2 dm.

$$[\alpha] = 18{\cdot}454/(\lambda^2 - 0{\cdot}08225) + 8{\cdot}346/\lambda^2.$$

λ.	[α], obs.	[α], calc. − [α], obs.	Soltn.	λ.	[α], obs.	[α], calc. − [α], obs.	Soltn.
6438	75·64°	0·02°	a	4358	215·29°	0·00°	a
5893	93·68	0·00	a	4356	215·80	−0·15	b
5780	98·34	−0·08	a	4167	248·91	1·08	b
5461	113·49	−0·35	a	4095	266·96	−1·19	b
5086	136·92	−0·04	a	3996	290·64	0·00	b
4800	160·73	0·07	a	3867	336·19	−6·12	b
4678	173·64	−0·41	a	3768	375·32	−7·56	b
4673	174·11	−0·31	b				

Rotatory Dispersion of Campholic Aldehyde in Chloroform at 20°.

$$[\alpha] = 18{\cdot}276/(\lambda^2 - 0{\cdot}08227) + 7{\cdot}985/\lambda^2.$$

(a) c = 13·368 g./100 c.c., l = 2 dm.; (b) c = 12·740 g./100 c.c., l = 2 dm.; (c) c = 12·270 g./100 c.c., l = 1 cm.; (d) c = 1·44; (e) c = 0·720; (f) c = 0·530; (g) c = 0·510; (h) c = 0·246 g./100 c.c., l = 1 cm.

λ.	[α], obs.	[α], calc. − [α], obs.	Soltn.	λ.	[α], obs.	[α], calc. − [α], obs.	Soltn.
6708	67·33°	0·12°	a	6497	72·35°	0·35°	a
6438	74·22	0·04	a	6362	76·52	−0·13	a
6104	84·35	0·05	a	5893	91·99	0·00	a
5782	96·38	0·01	a	5780	96·49	−0·01	a
5700	100·09	−0·20	a	5536	107·80	−0·23	a
5472	111·30	−0·25	a	5461	111·77	−0·35	a
5218	125·37	0·09	a	5209	126·10	−0·01	a
5153	129·91	−0·13	a	5105	133·26	−0·18	a
5086	134·50	0·00	a	4934	145·40	0·79	a
4810	157·08	−0·03	a	4800	157·50	0·55	a
4722	165·80	−0·10	a	4680	169·64	0·45	a
4678	170·00	0·30	a	4554	184·50	0·06	b
4358	212·25	−0·49	a	4549	184·6	0·65	b
4271	224·8	1·46	b	4070	266·0	1·47	b
3876	322·8	−0·73	b	3872	323·4	0·00	b
3756	373·9	−6·53	b	3713	393·7	−10·82	b
3674	413·2	−7·31	b				

Region of absorption.

λ.	[α], obs.	Soltn.	λ.	[α], obs.	Soltn.
3739	369·3	c	3670	411·0	c
3517	513·8	c	3459	584·0	c
3450 } 3125	597	e	3426	649·5	c
			3425	653	d
3406	690·0	c	3382	730·0	c
3355 } 3144	806	e	3347 } 3134	800	d
3250 } 3180	901	e	3220	950	f
			3091	302	f
3067	157	g	3018	0	ef
2936	−157	g	2853	−302	g
2860	−320	e	2787	−470	g
2770	−497	e	2540	−320	h
2755	−500	g			

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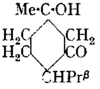
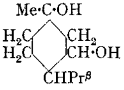
41. *Researches in the Menthone Series. Part XIV.* dl-1-*Hydroxymenthone,* dl-*Menthane*-1 : 3-*diols, and* dl-Δ^6-neo*Menthen*-3-*ol.*

By John Read and Geoffrey Swann.

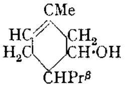
Its resistance to oxidation by Beckmann's reagent, as noted below, indicates that the *dl*-hydroxymenthone resulting from the catalytic hydrogenation of *dl*-piperitone oxide (Walker and Read, J., 1934, 241) is *dl*-1-hydroxymenthone (I): the alternative 2-hydroxymenthone would yield diosphenol in this way. Further hydrogenation of this substance furnished a mixture of dl-*menthane*-1 : 3-*diols* (II), of which four stereoisomeric *dl*-forms are possible. One of these, m. p. 143°, has been isolated and characterised by means of its 3 : 5-dinitrobenzoate, m. p. 199—200.°



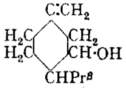
(I.)



(II.)



(III.)



(IV.)

Dehydration of the mixture of diols yielded an unsaturated menthen-3-ol, which was converted by hydrogenation into a mixture of menthols. One of these was identified as *dl-neo*menthol, and the other was therefore *dl-neoiso*menthol (Read and Grubb, J., 1934, 1779). Consequently, the menthenol in question belonged to the *neo*-series, with *cis*-H atoms in positions 3 and 4. From its method of formation, this menthenol must be Δ^1, Δ^6, or $\Delta^{1(7)}$. It showed none of the characteristic properties of Δ^1-menthen-3-ol (piperitols; see J., 1930, 2770; 1934, 308), and it resisted oxidation with Beckmann's reagent; it displayed no marked exaltation of molecular refractivity, characteristic of a semicyclic double bond; moreover, upon ozonisation it furnished only a little formaldehyde. Thus the alcohol was apparently dl-Δ^6-neo*menthen*-3-*ol* (III), with possibly a small amount of $\Delta^{1(7)}$-*neo*menthen-3-ol (IV), into which it may conceivably isomerise under favourable conditions.

Little, if anything, seems to be known of βγ-unsaturated alicyclic alcohols, and further investigations will be necessary in order to determine whether reluctant oxidation to the corresponding ketone is a characteristic of the type. Incidentally, the Δ^6-menthen-3-one obtained in an impure condition from this alcohol appears to be the first known example of a monocyclic terpene ketone with an endocyclic double bond which is not in the αβ-position.

Experimental.

dl-1-*Hydroxymenthone*.—This substance was prepared by the catalytic hydrogenation of *dl*-piperitone oxide, either by the method of Walker and Read (J., 1934, 241) or in presence of other suitable low-temperature catalysts. It crystallised in colourless prisms, m. p. 89—90°. The faces of the crystals were too dull and uneven to permit of goniometric characterisation. Prof. H. L. Bowman, Department of Mineralogy, University of Oxford, reported that they were probably orthorhombic: "a combination of a bipyramid with two pinakoid forms, resembling the rhombic dodecahedron, but one of the pinakoids has nearly square faces. The optic axial plane is parallel to the square pinakoid faces, and the negative acute bisectrix is normal to the other pinakoid. There are no faces present which would throw any light on the question of enantiomorphism."

dl-1-Hydroxymenthone resisted oxidation with Beckmann's reagent (*Annalen*, 1889, **250**, 335). When heated with its own weight of potassium bisulphate at 135° for 30 minutes, it yielded *dl*-piperitone; also when heated on the water-bath in aqueous alcoholic solution with the acetate of hydroxylamine or semicarbazide, it yielded, respectively, the oxime and semicarbazone of *dl*-piperitone. The *semicarbazone*, prepared in cold aqueous alcohol, formed long, colourless needles, m. p. 190—190·5° (Found: C, 58·3; H, 9·3. $C_{11}H_{21}O_2N_3$ requires C, 58·1; H, 9·3%). The crude oxime, prepared similarly, melted at 94—98°, and was too soluble to permit of fractional recrystallisation. The p-*nitrobenzoate* crystallised from methyl alcohol in yellow needles, m. p. 109° (Found: C, 63·9; H, 6·7. $C_{17}H_{21}O_5N$ requires C, 63·9; H, 6·6%). The *l*-menthoxyacetate was a syrup.

dl-*Menthane*-1 : 3-*diols*.—In presence of suitable catalysts at about 7 atm. pressure it proved possible to hydrogenate *dl*-piperitone oxide either to the above *dl*-1-hydroxymenthone (at 30—

35°) or to continue to the diol stage (at 65°), with the respective uptake of 2 or 4 hydrogen atoms per molecule. The second fraction obtained upon distilling the product of the complete hydrogenation formed a very viscid, odourless oil, b. p. 129—138°/12·5 mm., $n_D^{19°}$ 1·4730 (Found : C, 69·8; H, 11·5. $C_{10}H_{20}O_2$ requires C, 69·3; H, 11·6%). When treated in pyridine with *p*-nitro- or 3 : 5-dinitro-benzoyl chloride (1 or 2 mols.), this mixture of *diols* yielded syrupy or vitreous products. A *monoacetate* was obtained similarly as a thick oil, b. p. 130—136°/17 mm., $n_D^{18°}$ 1·4585 (Found : C, 67·3; H, 10·4. $C_{12}H_{22}O_3$ requires C, 67·3; H, 10·3%). Beckmann's reagent oxidised the mixture of diols to the above *dl*-1-hydroxymenthone, m. p. 89—90°.

The product obtained by the catalytic hydrogenation of purified *dl*-1-hydroxymenthone crystallised partly when kept. When it was washed with ether–light petroleum and recrystallised five times from acetone, a homogeneous dl-*menthan*-1 : 3-*diol* separated in small colourless crystals, m. p. 143° (Found : C, 70·1; H, 11·6%).

The crystalline diol reacted with *p*-nitrobenzoyl chloride to form a glass, but the 3 : 5-*dinitrobenzoate* separated from methyl alcohol in yellow prisms, m. p. 199—200° (decomp.) (Found : C, 51·7; H, 4·3. $C_{24}H_{24}O_{12}N_4$ requires C, 51·4; H, 4·3%).

dl-Δ^6-neo*Menthen*-3-*ol*.—The above mixture of diols was heated with its own weight of potassium bisulphate at 140° for 30 minutes : the product yielded about 15% of a terpene fraction and 45% of an alcohol fraction, when distilled, the remainder being unchanged diol. Treatment with 20% aqueous oxalic acid on a boiling water-bath for 2 hours was preferred, as it gave about 25% of terpene (b. p. to 99°/12 mm., $n_D^{16°}$ 1·4691) and 45% of alcohol. The latter fraction had b. p. 99—104°/12 mm., 100—108°/19 mm., $n_D^{16°}$ 1·4750, $n_D^{19°}$ 1·4724. Unsatisfactory results were obtained by heating the diol with anhydrous copper sulphate in ligroin, *d*-camphor-10-sulphonic acid in dry benzene, or acetic anhydride. When the alcohol fraction was esterified in dry pyridine with 3 : 5-dinitrobenzoyl chloride, it gave a 60% yield of crude ester; upon fractional recrystallisation from methyl alcohol–ethyl acetate (3 : 1), about one-third of this was obtained in yellow prisms, m. p. 118—119° (Found : C, 58·8; H, 5·8. $C_{17}H_{20}O_6N_2$ requires C, 58·6; H, 5·8%). The dl-Δ^6-neo*menthen*-3-*yl* 3 : 5-*dinitrobenzoate* so prepared was readily hydrolysed when heated under reflux with 2·5% methyl-alcoholic potassium hydroxide. The resulting dl-Δ^6-neo*menthen*-3-*ol* was a colourless, odourless, mobile oil, b. p. 99°/17·5 mm., $n_D^{15°}$ 1·4792, $n_D^{18°}$ 1·4783, $d_{4°}^{15°}$ 0·9346, $[R_L]_D$ 46·78 (calc. for $C_{10}H_{18}O$, 1 $|^=$, 47·2). Another specimen had $n_D^{15°}$ 1·4800, $d_{4°}^{15°}$ 0·9343, $[R_L]_D$ 46·94 (Found : C, 77·4; H, 11·4. $C_{10}H_{18}O$ requires C, 77·9; H, 11·7%). The *p*-nitrobenzoate was a white, micro-crystalline powder, m. p. 82—83°; it was phototropic and became yellow when exposed to bright light. The *d*-camphor-10-sulphonate was too soluble to permit of recrystallisation.

Upon hydrogenation at room temperature in methyl alcohol containing a 2% palladised calcium carbonate catalyst (compare J., 1934, 241), the above menthenol yielded an oil smelling of menthol. The derived 3 : 5-dinitrobenzoate, after several recrystallisations from methyl alcohol, furnished a fraction consisting of pale yellow needles, m. p. 129—130°. Mixtures of this substance with *dl-iso*menthyl 3 : 5-dinitrobenzoate (m. p. 130°) and *dl-neo*menthyl 3 : 5-dinitrobenzoate (m. p. 130°; J., 1933, 170) melted at 112° and 130°, respectively : the substance was thus *dl-neo*menthyl 3 : 5-dinitrobenzoate.

When oxidised with Beckmann's reagent under widely varied conditions, the menthenol yielded products which, although partly ketonic, appeared to vary in composition. In an oxidation conducted below 75°, the black chromium compound broke up only partially, and yielded a yellow oil with a strong odour, b. p. 93—95°/17 mm., $n_D^{17°}$ 1·4711. The derived *semicarbazone* was not homogeneous : a purified specimen crystallised from methyl alcohol in yellow prisms, m. p. 179—180° (Found : C, 63·4; H, 9·0. $C_{11}H_{19}ON_3$ requires C, 63·2; H, 9·1%). Another fraction of semicarbazone consisted of a white powder, m. p. *ca.* 200°. The oxime was a viscid syrup. Chromic anhydride in glacial acetic acid and potassium permanganate in acetone failed to oxidise the menthenol. Upon oxidation with 5% aqueous alkaline potassium permanganate (compare Simonsen, J., 1921, 119, 1653), the menthenol gave rise to an acidic product consisting of a thick brown oil which would not crystallise even after fractional distillation in a vacuum; neither formaldehyde nor formic acid was detected among the oxidation products.

An ozonisation of the above *dl*-Δ^6-*neo*menthen-3-yl 3 : 5-dinitrobenzoate, m. p. 118—119°, which was kindly undertaken for us by Prof. J. L. Simonsen, F.R.S., gave only a small quantity of formaldehyde, and decomposition of the ozonide yielded very little neutral product.

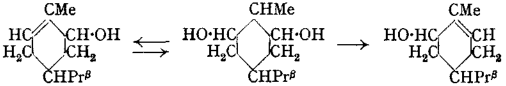
We are indebted to the Carnegie Trust for the Universities of Scotland for the award of a Research Scholarship to one of us (G. S.), and to Imperial Chemical Industries, Ltd., for a grant.

THE UNIVERSITY, ST. ANDREWS. [*Received, December 19th,* 1936.]

42. *Researches in the Carvone Series. Part IV. Optically Active Carvotanacetols and Carvotanacetylamines.*

By JOHN READ and GEOFFREY SWANN.

NEITHER of the two stereoisomeric carvotanacetols related to *d* (or *l*)-carvotanacetone has hitherto been isolated, although an impure carvotanacetol has been prepared by oxidising carvomenthene with selenium dioxide (Tabuteau, *Compt. rend.*, 1935, **200**, 244). It is now shown that Ponndorf's reduction (*Z. angew. Chem.*, 1926, **39**, 138) produces capricious results when applied to *d*-carvotanacetone (cf. J., 1935, 1140). An apparently pure d-*carvotanacetyl* p-*nitrobenzoate*, m. p. 93·5—94°, $[\alpha]_D$ + 85·0°, prepared from the reduction product, yielded upon hydrolysis a d-*carvotanacetol* with α_D + 100·5° (*l* 1); the pure *p*-nitrobenzoate of the stereoisomeric carvotanacetol, m. p. 60—62°, $[\alpha]_D$ − 51·3°, also appears to have been isolated. Unexpectedly, the above *d*-carvotanacetol (I) was found to undergo partial racemisation in presence of acids. This striking phenomenon, shown by a substance whose molecule contains two dissimilar asymmetric centres in a ring system, may be due either (1) to hydration to the 2 : 6-diol (II),* followed by a two-way dehydration, as indicated below,

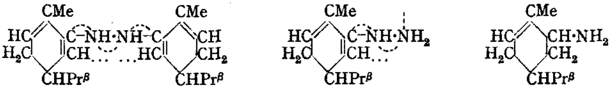


(I, *d*-form.) (II.) (I, *l*-form.)

or (2) to anion migration, which might apply to the nitrobenzoates as well as to the free alcohols (cf. such references as Burton and Ingold, J., 1928, 90; Burton, J., 1928, 1650; 1930, 248; 1934, 1268—for which we are indebted to Dr. J. Walker). Further, we find that *l*-*trans*-carveol (J., 1934, 236) and *l*-Δ^4-menthen-3-ol (unpublished) suffer partial racemisation in presence of acids, as might be inferred from their structural likeness to the carvotanacetols.

It is striking that this carvotanacetol showed no tendency to undergo dehydration to α-phellandrene, like the structurally related αβ-unsaturated piperitols (J., 1930, 2770; 1934, 308). Indeed, the investigations recorded in this paper and the preceding one serve to illustrate how little is known of the behaviour of unsaturated monocyclic alcohols.

When treated with hydrazine, *d*-carvotanacetone reacted very similarly to *l*-piperitone (J., 1930, 2770), yielding a viscid product which appeared to consist of a mixture of the azine and the hydrazone. Upon reduction with tin and acetic acid, this gave a mixture of carvotanacetylamines (V), which, however, differed from the corresponding piperitylamines (*ibid.*) in being optically active. This interesting result confirms the mechanism postulated earlier (J., 1934, 310) for the reduction of piperitone azine, since in the present instance the supposed lactam form of the azine (III), or hydrazone (IV), would not lose its asymmetry :



(III.) (IV.) (V.)

A similar mixture of two stereoisomeric carvotanacetylamines was obtained by reducing *d*-carvotanacetone oxime (Harries and Johnson, *Ber.*, 1905, **38**, 1832). The crude base, having α_D + 121·46° (*l* 1), when treated with *d*-tartaric or oxalic acid readily yielded pure d-*carvotanacetylamine*, with α_D + 169·54°. The benzoyl derivative of this base had m. p. 97—98°, $[\alpha]_D$ + 214·0° (*c* 2·0, chloroform). The benzoyl derivative of the stereoisomeric

* The diagram applies to the two *dl*-forms of the asymmetric *trans*-2 : 6-diol : both forms of the *cis*-2 : 6-diol would be symmetric.

base was also isolated, and this derivative had m. p. 165°, $[\alpha]_D - 87.5°$. No stereochemically pure carvotanacetol has as yet been prepared from the above *d*-carvotanacetylamine by methylation or through the action of nitrous acid (cf. J., 1930, 2779).

Experimental.

The Reduction of d-*Carvotanacetone to Carvotanacetols.*—*d*-Carvone from caraway oil was hydrogenated with the aid of a selective catalyst until 1 mol. of hydrogen had been absorbed. Purification of the product by means of the bisulphite compound yielded a pale yellow, mobile oil with an odour resembling that of *d*-carvone; the main fraction, distilling at 98—99°/16 mm., gave constants, $n_D^{21°}$ 1·4791, $[\alpha]_D^{19°} + 55.2°$, agreeing well with the published data for *d*-carvotanacetone. The ketone reacted with semicarbazide acetate in cold aqueous alcoholic solution, yielding a semicarbazone (80% yield) with m. p. 170—171°, $[\alpha]_D + 77.0°$ (*c* 2·0 chloroform). After several recrystallisations this product furnished large colourless prisms, m. p. 173—174°, $[\alpha]_D + 80.0°$. When hydrolysed with hot 20% aqueous oxalic acid, the derivative yielded *d*-carvotanacetone with b. p. 105—106°/21·5 mm., $n_D^{20°}$ 1·4796, $[\alpha]_D + 58.3°$. The purified oxime had m. p. 76—77°, $[\alpha]_D + 22.5°$ (*c* 2·0, chloroform). The 2 : 4-*dinitrophenylhydrazone* formed scarlet needles, m. p. 191—192°.

Upon reduction with dry *iso*propyl alcohol and aluminium *iso*propoxide for 8—9 hours, according to the method of Ponndorf (*Z. angew. Chem.*, 1926, **39**, 141), *d*-carvotanacetone having $[\alpha]_D^{19°} + 55.2°$ gave a product which distilled mainly at 108—109°/19·5 mm., and had $n_D^{20°}$ 1·4800, $\alpha_D^{18°} + 86.0°$ (*l* 1, homogeneous). The derived 3 : 5-dinitrobenzoate was a solid with $[\alpha]_D + 61.0°$ (*c* 2·0, chloroform), which could not be effectively recrystallised. The crude *p*-nitrobenzoate had m. p. 87—90°, $[\alpha]_D + 76.5°$; when it was recrystallised four times from methyl alcohol, the values for the resulting d-*carvotanacetyl* p-*nitrobenzoate* reached constancy at m. p. 93·5—94°, $[\alpha]_D + 85.0°$ (Found: C, 67·3; H, 6·9. $C_{17}H_{21}O_4N$ requires C, 67·3; H, 6·9%). Hydrolysis with boiling 3·5% methyl-alcoholic potassium hydroxide yielded d-*carvotanacetol* as a somewhat viscid oil, b. p. 101°/13 mm., $n_D^{20°}$ 1·4800, $\alpha_D^{17°} + 100.5°$ (*l* 1, homogeneous), $d_4^{17°}$ 0·9307, $[R_L]_D$ 47·1 (calc. for $C_{10}H_{18}O$, $1|^{=}$, 47·3).

Oxidation of the above alcohol with Beckmann's mixture furnished a ketone with b. p. 96·5°/14 mm., $n_D^{19°}$ 1·4800, $\alpha_D^{17°} + 40.7°$ (*l* 1, homogeneous). This specimen of *d*-carvotanacetone thus contained some *dl*-carvotanacetone, and fractional crystallisation of the derived semicarbazone furnished a fraction with m. p. 180—181°, $[\alpha]_D + 3.7°$ (*c* 2·0, chloroform). Pure *dl*-carvotanacetone semicarbazone, prepared from the *dl*-ketone, crystallised in prisms, m. p. 180°, and *dl*-carvotanacetone oxime in stout needles, m. p. 94—95°.

In tracing the point at which the partial racemisation had occurred, it was found that the optical rotation of *d*-carvotanacetone was not disturbed by submitting the ketone to the conditions of the Beckmann oxidation at 60°. The optical rotation of the mixture of alcohols obtained in a Ponndorf reduction of this ketone, and having $\alpha_D^{18°} + 77.3°$ (*l* 1, homogeneous), also remained unaltered when the mixture was kept in contact with 2*N*-sodium hydroxide solution at 90° for 15 minutes. When this treatment was repeated with 12% hydrochloric acid, however, the optical rotation fell from $\alpha_D^{18°} + 77.3°$ to $+ 12.8°$; a small quantity of *dl*-α-phellandrene was produced during this treatment. Another specimen of this mixture of carvotanacetols when oxidised with Beckmann's mixture yielded *d*-carvotanacetone with $\alpha_D^{18°} + 44.0°$: since the original ketone used in the Ponndorf reduction had $\alpha_D^{18°} + 52.0°$, it is evident that partial racemisation occurs during the oxidation of these carvotanacetols with chromic acid. It was shown further that the mixture of optically active carvotanacetols could be esterified in dry pyridine with 3 : 5-dinitrobenzoyl chloride and regenerated by alkaline hydrolysis without loss of optical rotation, provided that the reaction mixtures were not permitted to become acidic at any stage of the operations.

The above specific rotatory powers were the highest observed for *d*-carvotanacetyl *p*-nitrobenzoate and the corresponding *d*-carvotanacetol. Certain specimens of the ester with somewhat lower optical rotations failed to yield higher values upon repeated recrystallisation, thus indicating the possible formation of mixed crystals.

In one experiment, a specimen of *d*-carvotanacetone having $\alpha_D + 54.44°$ (*l* 1), which had been regenerated from the purified semicarbazone (see above), yielded in the Ponndorf reduction a mixture of carvotanacetols with b. p. 113—114°/22 mm., $n_D^{18°}$ 1·4818, $\alpha_D + 50.89°$ (*l* 1). The crude *p*-nitrobenzoate had m. p. 50—80°, $[\alpha]_D - 1.0°$ (*c* 2·0, chloroform); six successive recrystallisations from methyl alcohol yielded needles, m. p. 93—94°, $[\alpha]_D + 85.2°$ (*c* 2·0 chloroform), identical with the *d*-carvotanacetyl *p*-nitrobenzoate already described. The first two mother-

liquors deposited needles, m. p. 57—63°, $[\alpha]_D$ − 44·2°; three successive recrystallisations from methyl alcohol yielded an isomeric *carvotanacetyl* p-*nitrobenzoate*, m. p. 60—62°, $[\alpha]_D$ − 51·3° (Found : C, 67·4; H, 6·8%). The crude 3 : 5-dinitrobenzoate, having m. p. 68—75°, $[\alpha]_D$ + 7·0°, after four recrystallisations from methyl alcohol yielded small yellow plates of a *carvotanacetyl* 3 : 5-*dinitrobenzoate*, m. p. 88·5—90°, $[\alpha]_D$ − 33·3° (Found : C, 58·7; H, 5·7. $C_{17}H_{20}O_6N_2$ requires C, 58·6; H, 5·8%). The mother-liquors yielded a white powder. The above Ponndorf reduction, furnishing a mixture of carvotanacetols of exceptionally low rotatory power, could not be repeated.

The Preparation of Carvotanacetylamines from d-*Carvotanacetone*.—(1) *d*-Carvotanacetone oxime (50 g.), having $[\alpha]_D$ + 22·5° (*c* 2·0, chloroform), was dissolved in absolute alcohol (100 c.c.) and mixed at 0° with glacial acetic acid (200 c.c.). Pure zinc powder (80 g.) was introduced gradually (2 hours) into the stirred mixture, which was kept below 5°, and after an hour more acetic acid (25 c.c.) was added (cf. Harries and Johnson, *Ber.*, 1905, **38**, 1832). Stirring was continued before (1 hour) and after ($2\frac{1}{2}$ hours) removing the mixture from the ice-bath. The temperature rose spontaneously to 60°, and the reaction was completed by heating the mixture on a boiling water-bath (1 hour). The product was cooled and filtered, the residue being washed with water and methyl alcohol. The ice-cooled filtrate was basified with concentrated sodium hydroxide solution and distilled in steam. The acidified distillate was extracted twice with ether, basified, saturated with potassium chloride, and again extracted twice with ether. The last extracts, when dried and distilled, yielded the crude base (30 g.) with b. p. 97°/17·5 mm., $n_D^{15°}$ 1·4820, $\alpha_D^{15°}$ + 121·46° (*l* 1, homogeneous). The crude hydrogen *d*-tartrate (143 g.) had m. p. 95—105°, $[\alpha]_D$ + 68·8° (*c* 2·0, water); after four recrystallisations from ethyl acetate–methyl alcohol, flat needles (52 g.) of d-*carvotanacetylamine hydrogen* d-*tartrate* were obtained, with m. p. 141—142°, $[\alpha]_D^{15°}$ + 97·5° (*c* 2·0, water), $[M]_D$ of basic ion + 249° (Found : C, 55·4; H, 8·3. $C_{14}H_{25}O_6N$ requires C, 55·4; H, 8·3%). The crude hydrogen oxalate had m. p. *ca.* 170°, $[\alpha]_D^{15°}$ + 75·0° (*c* 2·0, water); after three recrystallisations from ethyl acetate–methyl alcohol, minute needles of d-*carvotanacetylamine hydrogen oxalate* were obtained, with m. p. 205°, $[\alpha]_D^{15°}$ + 102·3° (*c* 2·0, water), $[M]_D$ of basic ion + 248° (Found : C, 59·6; H, 8·6. $C_{12}H_{21}O_4N$ requires C, 59·3; H, 8·5%). The original mother-liquors from the above recrystallisations yielded thick syrups upon evaporation. Pure *d*-carvotanacetylamine was obtained by treating the above pure hydrogen *d*-tartrate with aqueous sodium hydroxide. A colourless mobile liquid with a basic odour, it absorbed carbon dioxide rapidly from the air, and had b. p. 93°/16·5 mm., $d_4^{15°}$ 0·8917, $n_D^{15°}$ 1·4815, $n_D^{16·5°}$ 1·4810, $\alpha_D^{15°}$ + 169·54°, $[\alpha]_D^{15°}$ + 190·1° (*l* 1, homogeneous), $[R_L]_D$ 48·92 (calc. for $C_{10}H_{19}N$, $1|^{=}$, 49·13).

Acetyl-d-*carvotanacetylamine* crystallised in flat needles, m. p. 112°, $[\alpha]_D$ + 155·3° (*c* 2·0, chloroform) (Found : C, 73·9; H, 10·8. $C_{12}H_{21}ON$ requires C, 73·8; H, 10·8%). *Benzoyl*-d-*carvotanacetylamine* formed long needles, m. p. 97—98°, $[\alpha]_D$ + 214·0° (*c* 2·0, chloroform) (Found : C, 79·7; H, 8·8. $C_{17}H_{23}ON$ requires C, 79·3; H, 9·0%). The hydrogen succinate was obtained crystalline, but the hydrogen phthalate formed a viscid syrup.

(2) When treated with hydrazine, according to the method of Read and Storey (J., 1930, 2780), *d*-carvotanacetone gave a fairly mobile, pale yellow syrup having $[\alpha]_D^{17°}$ + 11·5° (*c* 2·3, chloroform) (Found : C, 73·1; H, 10·5; N, 14·8%). After remaining at the ordinary temperature for 14 days the material had become much more viscid and the colour had deepened to a dark red-brown; the value of $[\alpha]_D^{17°}$ had meanwhile changed to − 47·9° (Found : C, 73·9; H, 10·2; N, 13·6. Carvotanacetone hydrazone, $C_{10}H_{18}N_2$, requires C, 72·3; H, 10·8; N, 16·9. Carvotanacetone azine, $C_{20}H_{32}N_2$, requires C, 80·0; H, 10·8; N, 9·3%).

When the freshly prepared material was reduced by the method of Read and Storey (*loc. cit.*) it gave a 25% yield of a base resembling that obtained by the reduction of *d*-carvotanacetone oxime and having b. p. 100—102°/24·5 mm., $n_D^{21°}$ 1·4792, $\alpha_D^{17°}$ + 106·3° (*l* 1, homogeneous). The crude benzoyl derivative was a pasty mass with $[\alpha]_D^{16°}$ + 87·5° (*c* 2·0, chloroform); six recrystallisations from methyl alcohol yielded long needles of a second *benzoylcarvotanacetylamine*, with m. p. 165°, $[\alpha]_D$ − 87·5° (*c* 2·0, chloroform) (Found : C, 79·5; H, 8·7. $C_{17}H_{23}ON$ requires C, 79·3; H, 9·0%). The same derivative was obtained similarly from crude *d*-carvotanacetylamine having $\alpha_D^{14°}$ + 118·60° (*l* 1, homogeneous), prepared from *d*-carvotanacetone oxime as in (1) above.

Catalytic Hydrogenation of d-*Carvotanacetylamine Hydrogen* d-*Tartrate*.—A solution of this salt (6 g.) in methyl alcohol (150 c.c.) was hydrogenated in presence of a 2% palladised calcium carbonate catalyst (10 g.) for 45 minutes at a pressure of 3 atms. The residual salt had m. p. 150—160°, $[\alpha]_D^{17°}$ + 2·0° (*c* 2·0, water). Four recrystallisations from water containing a little methyl alcohol yielded a substance with m. p. 177—178°, $[\alpha]_D^{17°}$ + 6·0° (*c* 2·0, water). Admixture

of this substance with authentic l-isocarvomenthylamine hydrogen d-tartrate (*J.*, **1935**, **1143**) *did not affect the melting point.* No other pure substance could be isolated from the mother-liquors.

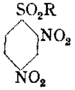
We are indebted to the Carnegie Trust for the Universities of Scotland for the award of a Research Scholarship to one of us (G. S.), to Imperial Chemical Industries, Ltd., for a grant, and to Messrs. Howards and Sons, Ltd., Ilford, for the carvotanacetone used in this research.

THE UNIVERSITY, ST. ANDREWS. [*Received, December 19th*, 1936.]

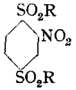
43. *The Mobility of Groups in Certain Nitrodiphenylsulphones.*

By JAMES D. LOUDON and THOMAS D. ROBSON.

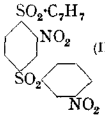
WHEN cationoid reactivity is displayed by nitrobenzene derivatives the reactive centres are generally those situated *o*- or *p*- to the nitro-group which, among *m*-directing groups, is pre-eminent in its power to produce activation of this type. It has, nevertheless, been observed in certain isolated cases, where in the same molecule the effects of a nitro- and of a second activating group appear to be in competition with each other, that either the nitro-group itself (*e.g.*, *o*- and *p*-nitrocyanobenzenes, Reinders and Ringer, *Rec. trav. chim.*, 1899, **18**, 326, 330; 2-chloro-4-nitrobenzaldehyde, Tiemann, *Ber.*, 1891, **24**, 709; 2 : 4 : 6-trinitrobenzylideneaniline, Secareanu, *Ber.*, 1931, **64**, 837) or another substituent *o*- or *p*-to the second group (*e.g.*, 2 : 6-dichloro-4-nitrobenzenediazonium hydroxide; Witt, *Ber.*, 1909, **42**, 2957) undergoes replacement. This apparent transference of activation control or of activated centre is probably occasioned, in part at least, by reluctance of the second activating group itself to undergo replacement, and the point is aptly illustrated by the behaviour of 2 : 4-dinitrodiphenylsulphones (I), in which, by use of sulphinates as reagents, virtual immobility may be conferred on the otherwise labile sulphonyl group and production of (II) results (Loudon, *J.*, 1936, 218; R = *p*-tolyl and phenyl). Other circumstances both internal and external to the molecule may be expected to contribute in determining the locus and degree of mobility displayed, and we have sought further information by extending the reaction (I ⟶ II), and by examining the effects produced on the mobility by certain modifications of the structure (I).



(I.)



(II.)

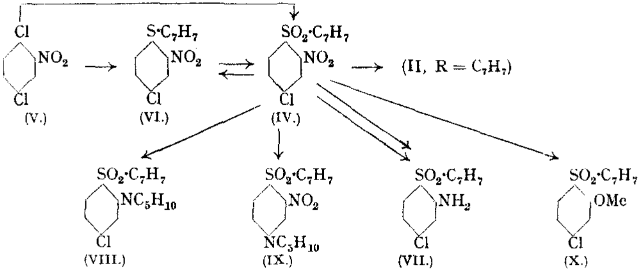


(III.)

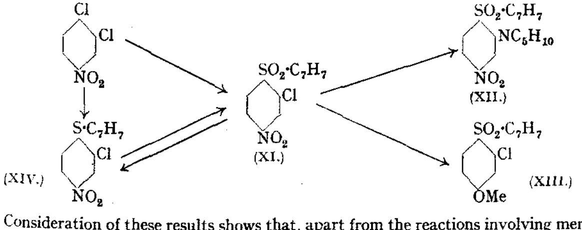
Under equilibrium conditions the ease with which sulphonyl groups replace each other may be represented by the order $p\text{-}CH_3 \cdot C_6H_4 \cdot SO_2 > C_6H_5 \cdot SO_2 > p\text{-}C_6H_4Cl \cdot SO_2 > m\text{-}NO_2 \cdot C_6H_4 \cdot SO_2 > 2:5\text{-}C_6H_3Cl_2 \cdot SO_2$ (*J.*, 1935, 896), and we have found that the same qualitative order also represents the speeds of reactions (I ⟶ II). For instance, 4-chloro-2 : 4-dinitrodiphenyl-sulphone (I, R = C_6H_4Cl) with sodium *p*-chlorobenzenesulphinate yielded (II, R = C_6H_4Cl), identical with a specimen synthesised from chlorobenzene and 4-chloro-3-nitrobenzene-sulphonyl chloride, followed by condensation with the sulphinate. On the other hand, with R = 2 : 5-dichlorophenyl, no disulphonyl compound (II) could be detected even under more intense reaction conditions. The reaction of sodium *p*-toluenesulphinate on (III) was selected as a favourable case for investigating the replacement of a sulphonyl group instead of a nitro-group as potential anion. Under comparable conditions, however, no reaction took place and prolonged treatment caused destruction of the materials.

Interesting results were obtained by extending the investigation to the *halogen* compound (IV), which was prepared either directly from (V) or *via* the *sulphide* (VI). It was found that, according to the reagent employed, any one of the three potential anions could be replaced. With sodium *p*-toluenesulphinate the chlorine atom was replaced, (II,

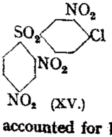
$R = C_7H_7$) being formed as readily as from (I). Methyl-alcoholic ammonia effected replacement of the nitro-group, the isolated *amine* (VII) being identical with the product of reduction. The sulphonyl group was replaced, with regeneration of (VI), by the action of *p*-thiocresol in presence of alkali. Further, brief treatment of (IV) with hot piperidine gave two separate *piperidino*-derivatives (VIII) and (IX)—4-chloro-2-nitropiperidinobenzene was obtained by Lellman and Geller (*Ber.*, 1888, **21**, 2283) from (V)—and finally, by the action of sodium methoxide on (IV), the nitrogen-free *ether* (X) was produced.



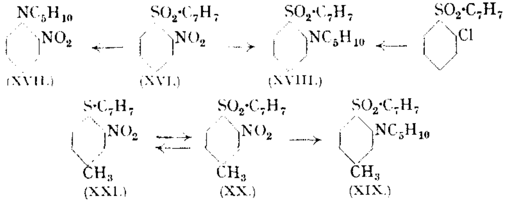
Slightly different results were obtained by the action of the same reagents on the isomeric *chloronitrosulphone* (XI). In this case no product could be isolated from the reaction with sodium *p*-toluenesulphinate, and with piperidine, only one *piperidino*-derivative (XII) was obtained, though here, as indeed in several other cases (cf. Experimental), indications were found that reaction was not confined to one centre. In contrast to the behaviour of (IV), treatment of (XI) with methyl-alcoholic ammonia yielded, instead of an amine, the *ether* (XIII), also obtained with sodium methoxide as reagent, and this resistance to attack by ammonia was further shown by recovery of the material (XI) unchanged from boiling acetamide (procedure, cf. Kym, *Ber.*, 1899, **32**, 3539). The reaction with *p*-thiocresol in presence of alkali was analogous to that found in the previous case, the *sulphide* (XIV) being formed.



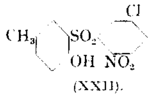
Consideration of these results shows that, apart from the reactions involving mercaptide (cf. also XX ⟶ XXI, below), *the groups replaced are those situated o- and p- to the* sulphonyl group. This differentiation between mercaptide and the other reagents is paralleled by work still unpublished and by experiments with (XV). Here with piperidine preferential replacement of chlorine occurs (J., **1935**, 537), whereas with a slight deficiency of mercaptide there resulted only 2 : 4-dinitrophenyl *p*-tolyl sulphide (m. p. and mixed m. p.) with mere traces of ionisable halogen. In the other reactions it is important *to note that the mobility is pronounced and is not adequately accounted for by the activating power of the sulphone group alone.* Thus, quantitative



comparison of the mobilities displayed by chlorine in *o*-, *m*-, and *p*-chlorophenylmethylsulphones with those in the corresponding chloronitrobenzenes (Todd and Shriner, *J. Amer. Chem. Soc.*, 1934, **56**, 1382) shows that the former compounds are decidedly less reactive and, qualitatively, we have also found that formation of (IX) and (XII) occurs very much more readily than the reaction between piperidine and *o*- or *p*-chlorophenyl-*p*-tolylsulphone. The reaction between piperidine and *o*-nitrophenyl-*p*-tolylsulphone (XVI) was also relatively slow and, moreover, gave rise to two *products* (XVII) and (XVIII).



This concurrent replacement of sulphonyl and nitro-groups by piperidine raises the question why, in similar treatment of (IV), the sulphonyl group has survived. It seems probable that partial answers may be found in the activating influence of an *op*-directing group on a potential anion in the *m*-position (Kenner, J., 1914, **105**, 2728; 1922, **121**, 489), and also in the complementary stabilisation of substituents in the *o*- and *p*-positions. For example, we could isolate only one *product* (XIX) from the action of piperidine on the *sulphone* (XX), which differs from (IV) in having methyl in place of chlorine—an alteration, incidentally, causing here, as in other recorded cases (cf. Ibbotson and Kenner, J., 1923, **123**, 1265), marked decrease in the degree of mobility displayed. With alkaline *p*-thiocresol, (XX) gave the *thioether* (XXI), but was recovered unchanged from heating with sodium methoxide in methyl alcohol. It is obvious that the reactivity of these systems is sensitive to a variety of influences and it may be noted that replacement of the nitro- in preference to the sulphonyl group in the majority of the reactions with (IV) is in contrast to the behaviour of (XXII) and similar sulphones studied by Smiles and his co-workers (*e.g.*, J., 1932, 2774; 1934, 422; 1935, 181). In presence of alkali the facile reaction here is an intramolecular replacement of sulphonyl by the phenoxy-group, and thioxin ring formation is apparently of a secondary order.



(XXII.)

It is hoped to make a more detailed study of certain aspects of the present work and further discussion is meantime postponed.

EXPERIMENTAL.

4 : 4′-*Dichloro-3-nitrodiphenysulphone*.—(A) Aluminium chloride (3 g.) was added to a hot solution of 4-chloro-3-nitrobenzenesulphonyl chloride (4 g.) in chlorobenzene (2 c.c.), and the mixture heated (100°) for 1 hour. The product obtained after cooling and pouring into water crystallised from alcohol or acetone in colourless prisms, m. p. 130°. (B) The same *compound* was obtained together with dinitrated material (cf. Groves and Turner, J., 1929, 509) from 4 : 4′-dichlorodiphenylsulphone (1·5 g.) in sulphuric acid (20 c.c.) by cautious addition of potassium nitrate (0·53 g.) dissolved in sulphuric acid (10 c.c.), the resulting mixture being fractionally crystallised from acetone (Found : N, 4·5. $C_{12}H_7O_4NCl_2S$ requires N, 4·3%).

4′-*Chloro-3-nitro-4-piperidinodiphenysulphone*, m. p. 80°, was prepared from the last compound in the usual way and was purified by slow cooling of its alcoholic solution from room temperature to 0° (Found : N, 7·5. $C_{17}H_{17}O_4N_2ClS$ requires N, 7·4%).

1-*Nitro-2 : 5-di-p-chlorobenzenesulphonylbenzene*.—(A) 4 : 4′-Dichloro-3-nitrodiphenylsulphone (1 mol.) and sodium *p*-chlorobenzenesulphinate (1 mol.) were refluxed in aqueous alcohol for 1 hour (B) 4′-Chloro-2 : 4-dinitrodiphenylsulphone (0·5 g.) and the sulphinate (2 g.) were boiled in ethylene glycol solution for a few minutes. In each case after precipitation of the product

with water and crystallisation from acetic acid the same *compound* was obtained in colourless felted needles, m. p. 231°, yielding the above piperidino-derivative on treatment with hot piperidine (Found : Cl, 14·9. $C_{18}H_{11}O_6NCl_2S_2$ requires Cl, 15·1%).

4-Chloro-2-nitro-4'-methyldiphenyl Sulphide (VI).—2 : 5-Dichloronitrobenzene (1·9 g.) in hot alcohol (10 c.c.) was treated with an alcoholic solution of *p*-thiocresol (1·24 g.) and sodium hydroxide (0·4 g.). Separation of the *product* commenced almost at once, but the mixture was warmed for some time before being allowed to cool. The resulting solid crystallised from acetic acid in large orange prisms, m. p. 121° (Found : N, 5·2. $C_{13}H_{10}O_2NClS$ requires N, 5·0%).

The same product was formed by similar treatment of the sulphone (IV).

4-Chloro-2-nitro-4'-methyldiphenylsulphone (IV).—(A) The sulphide (VI) was oxidised in acetic acid solution with an excess of hydrogen peroxide; the *product*, which partly separated on cooling, crystallised from alcohol in long needles, m. p. 124° (Found : N, 4·4. $C_{13}H_{10}O_4NClS$ requires N, 4·5%). (B) Molecular proportions of 2 : 5-dichloronitrobenzene and sodium *p*-toluenesulphinate were heated in the minimum quantity of ethylene glycol for 2 hours. The gummy solid which formed on cooling was fractionated from alcohol and yielded the soluble sulphone (IV) and the sparingly soluble 1-nitro-2 : 5-di-*p*-tolylsulphonylbenzene (II, R = C_7H_7; m. p. and mixed m. p. 220°). The latter compound was also formed by brief treatment of the sulphone (IV) with the sulphinate in boiling glycol.

2-Chloro-4-nitro-4'-methyldiphenyl sulphide (XIV), m. p. 122° (Found : N, 5·0. $C_{13}H_{10}O_2NClS$ requires N, 5·0%), and the corresponding *sulphone* (XI), m. p. 125° (Found : N, 4·4. $C_{13}H_{10}O_4NClS$ requires N, 4·5%), were produced by the methods described for their isomers.

2-Nitro-4-piperidino-4'-methyldiphenylsulphone (IX).—The sulphone (IV) was boiled for 3 minutes with excess of piperidine and, after cooling, addition of water yielded a solid which partly dissolved in cold concentrated hydrochloric acid and partly formed a colourless, sparingly soluble residue (hydrochloride?), readily hydrolysed by water to a yellow *solid*. The latter crystallised from alcohol in yellow plates, m. p. 183° (Found : N, 7·8. $C_{18}H_{20}O_4N_2S$ requires N, 7·8%).

4-Chloro-2-piperidino-4'-methyldiphenylsulphone (VIII).—The hydrochloric acid solution from the last experiment was neutralised with dilute aqueous ammonia and the precipitated solid was crystallised from alcohol. After removal of a small quantity of the yellow solid (IX, m. p. 180°) which separated first, the mother-liquor on dilution with water gave fine colourless needles, m. p. 121° after recrystallisation (Found : N, 4·3. $C_{18}H_{20}O_2NClS$ requires N, 4·0%).

4-Nitro-2-piperidino-4'-methyldiphenylsulphone (XII).—The sulphone (XI) was treated with piperidine in the usual way. The *product* crystallised from alcohol in lemon-yellow needles, m. p. 171°. Although no other product could be identified, both chloride and nitrite ions were formed in the reaction (Found : N, 7·7. $C_{18}H_{20}O_4N_2S$ requires N, 7·8%).

4-Chloro-2-amino-4'-methyldiphenylsulphone (VII).—(A) The sulphone (IV) was reduced with stannous chloride and hydrochloric acid in alcohol (cf. J., 1936, 220); the product crystallised from alcohol in colourless plates, m. p. 136°. (B) Treatment of the sulphone (2 g.) with methyl alcohol (10 c.c.) and concentrated aqueous ammonia (3 c.c.) at 150° for 10 hours gave the same *product*, m. p. and mixed m. p. 135—136°. Chloride and nitrite ions were formed in the process (Found : N, 5·2. $C_{13}H_{12}O_2NClS$ requires N, 5·0%).

2-Chloro-4-amino-4'-methyldiphenylsulphone, m. p. 165°, was obtained by reduction of the corresponding nitro-compound with stannous chloride and hydrochloric acid (Found : N, 5·1. $C_{13}H_{12}O_2NClS$ requires N, 5·0%).

4-Chloro-2-methoxy-4'-methyldiphenysulphone (X).—The sulphone (IV) was refluxed in a methyl-alcoholic solution of sodium methoxide for 15 minutes. Addition of water yielded a yellowish *solid*, which crystallised from alcohol (charcoal!) in colourless needles, m. p. 117°. Chloride ions were also formed in the reaction (Found : Cl, 12·1; S, 11·2. $C_{14}H_{13}O_3ClS$ requires Cl, 12·0; S, 10·8%).

2-Chloro-4-methoxy-4'-methyldiphenylsulphone (XIII) was similarly prepared from (XI) and was the only product which could be isolated from the action of methyl-alcoholic ammonia on (XI) (procedure as for VII B); m. p. 118° (Found : Cl, 12·2; S, 11·1. $C_{14}H_{13}O_3ClS$ requires Cl, 12·0; S, 10·8%).

2-Chloro-4'-methyldiphenylsulphone.—2-Amino-4'-methyldiphenylsulphone was subjected to Hodgson and Walker's modification of the Sandmeyer reaction (J., 1933, 1620). The *product*, which was rather difficult to purify, was repeatedly crystallised from alcohol, forming plates, m. p. 113° (Found : C, 58·3; H, 4·4. $C_{13}H_{11}O_2ClS$ requires C, 58·5; H, 4·1%).

2-Piperidino-4'-methyldiphenylsulphone (XVIII), m. p. 118° (from alcohol) (Found : N, 4·55. $C_{18}H_{21}O_2NS$ requires N, 4·4%), and *4-piperidino-4'-methyldiphenylsulphone*, m. p. 134° (from

alcohol) (Found : N, 4·5%), were obtained by refluxing the corresponding chlorosulphones with piperidine (6 c.c. per 1 g.) for 2—3 hours (or by heating for shorter periods in sealed tubes at 160°), followed by extraction of the product with hydrochloric acid.

Action of Piperidine on 2-Nitro-4'-methyldiphenylsulphone.—The reagents were refluxed for 1½ hours, and the product extracted with concentrated hydrochloric acid. A quantity of unchanged sulphone was removed. The solid obtained by treating the extract with ammonia was slowly crystallised from alcohol, forming a mixture of red and pale yellow crystals which were separated by hand. The red variety after further purification melted at 73°, mixed m. p. 75° with authentic 2-nitropiperidinobenzene. The yellow crystals after several crystallisations from alcohol became colourless, m. p. 114°, and were identified (mixed m. p. 114—116°) as 2-piperidino-4'-methyldiphenylsulphone.

Similar treatment of 4-nitro-4'-methyldiphenylsulphone produced much tarry matter and very little acid-soluble material. The bulk of the sulphone was recovered unchanged.

*2-Nitrodi-*p*-tolyl sulphide* (XXI) was obtained in the usual way from 4-chloro-3-nitrotoluene (or the sulphone XX), *p*-thiocresol, and sodium hydroxide; it formed yellow plates, m. p. 116° (Found: N, 5·5. $C_{14}H_{13}O_2NS$ requires N, 5·4%).

*2-Nitrodi-*p*-tolylsulphone* (XX), m. p. 132°, was formed when (XXI) was oxidised with hydrogen peroxide in acetic acid (Found : N, 4·86. $C_{14}H_{13}O_4NS$ requires N, 4·8%).

*2-Piperidinodi-*p*-tolylsulphone* (XIX).—The sulphone (XX) was refluxed with excess of piperidine for 1½ hours. The *product*, obtained by the usual procedure, crystallised from aqueous alcohol in colourless prisms, m. p. 148° (Found : N, 4·4. $C_{19}H_{23}O_2NS$ requires N, 4·25%).

Our thanks are due to the Chemical Society for a grant and to Mr. J. M. L. Cameron, who carried out micro-nitrogen estimations on several of the compounds described.

The University, Glasgow. [*Received, November 24th, 1936.*]

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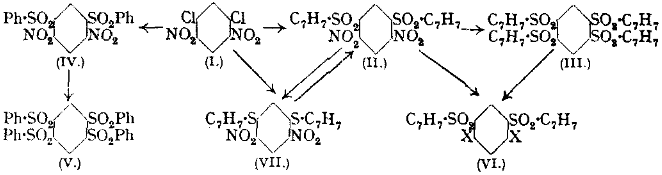
44. *The Action of Sulphinates on 1 : 5-Dichloro-2 : 4-dinitrobenzene.*

By A. Livingston and J. D. Loudon.

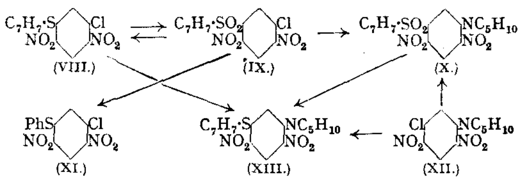
One interesting feature attending the use of sulphinates in displacing suitably activated substituents from a benzene nucleus consists in the fact that the sulphonyl groups so introduced may in turn activate new centres in the molecule and thus lead to further reaction. For instance, treatment of 2 : 4-dinitrochlorobenzene with sodium benzenesulphinate yields first 2 : 4-dinitrodiphenylsulphone and then 2 : 5-diphenylsulphonylnitrobenzene (Loudon, J., 1936, 218). Moreover, although the activating power of a single sulphonyl group may be slight (in comparison with nitro), yet by analogy with similar cases established by Schöpff and his co-workers (*Ber.*, 1891, **24**, 3771, 3785) it is to be anticipated that the combined effects of two such groups situated *meta* to each other will be considerable. From these points of view the action of sodium *p*-toluenesulphinate on 1 : 5-dichloro-2 : 4-dinitrobenzene (I) provides a case of particular interest, since here the arrangement of groups is such that ultimate production of tetra-*p*-tolylsulphonylbenzene may be expected. Experiment, in fact, showed that even under relatively mild conditions reaction proceeds beyond stage (II), yielding a mixture of sulphones from which the *tetrasulphone* (III) was isolated. The most interesting of the intermediate products, the *disulphonyl* compound (II), was obtained by employing in the reaction the free sulphinic acid instead of its salt—a modification which was unnecessary in the phenyl series (I ⟶ IV ⟶ V), since here under similar conditions the weaker replacing power of the benzenesulphinate (cf. J., 1935, 896) permitted isolation of (IV), the *tetrasulphone* (V) being formed only at higher temperatures.

The reactions of (II) with ammonia and piperidine also show the mobility of both nitro-groups. With the former reagent (II) and (III) each gave the *diamine* (VI, X = NH_2), also prepared from (II) by reduction, and similarly the *dipiperidino*-derivatives produced from (II) and (III) were identical (VI, X = NC_5H_{10}). On the other hand the sodium salt of *p*-thiocresol reacted with (II) to give the *dinitro-dithioether* (VII), directly obtained with this reagent from (I), thus providing another instance of the preferential replacement of

sulphonyl by mercaptide groups (cf. preceding paper). A similar selective action was also observed in the reactions of the *chlorodinitro-sulphone* (IX), which was obtained by oxidation of the *monothioether* (VIII) produced together with (VII) from (I). With theoretical



amounts of the reagents the chlorine atom was replaced by piperidine (IX ⟶ X), whereas alkaline *p*-thiocresol replaced the toluenesulphonyl group (IX ⟶ VIII). Since in reactions of the latter type the products might result from some unusual reduction of the sulphone group, we examined also the action of alkaline thiophenol on (IX) and, in harmony with the replacement view, obtained the *phenyl thioether* (XI), also directly prepared from (I). The other replacements depicted in the following scheme confirm the nature of the products referred to.



The results recorded here lend further support to the criticisms already advanced (Le Fèvre and Turner, J., *1927*, 1114, and refs. given) against the conclusions of Borsche and Bahr (*Annalen*, **1913**, **402**, 81), *viz.*, that there exists a fundamental difference in the mobilities of the two chlorine atoms in (I) [and correspondingly, in those of the nitro-groups in (II)]. Indeed, the ease with which both chlorine atoms are replaced renders difficult any qualitative assessment of the effect of the first replacement on the reactivity of the residual halogen. For this purpose, however, advantage was taken of the low replacing power of free *p*-toluenesulphinic acid as reagent and it was found that, of the compounds (IX) and (VIII or XII)—respectively derived from (I) by replacing one chlorine atom by a *m*-directing group on the one hand, and by a more powerful *op*-directing group (relative to Cl) on the other—the chlorine of (IX) alone underwent replacement. This result may be compared with the reappearance of suppressed halogen mobility following acetylation of certain chloronitroanilines (Lindemann and Pabst, *Annalen*, 1928, **462**, 24), and also with the fact that in the formation of (X) from (IX) by the action of piperidine the sulphonyl group has survived reaction conditions which occasion its replacement in the corresponding dinitrodiphenylsulphones (X; NC_5H_{10} replaced by H) (J., 1935, 537).

Experimental.

2 : 4-*Dinitro*-1 : 5-*di*-p-*tolylthiobenzene* (VII).—*p*-Thiocresol (2 mols.) and 1 : 5-dichloro-2 : 4-dinitrobenzene (1 mol.), dissolved in alcohol, were treated with a 10% solution of sodium hydroxide (2 mols.). The solid *product*, after crystallisation from acetic acid, formed yellow plates, m. p. 233° (Found : N, 7·0. $C_{20}H_{16}O_4N_2S_2$ requires N, 6·8%).

5-*Chloro*-2 : 4-*dinitro*-4′-*methyldiphenyl sulphide* (VIII) was obtained, after removal of (VII), as the more soluble product of a similar experiment in which molecular proportions of the

reagents were used and the temperature was maintained below 10°. It formed yellow needles, m. p. 147—148° (from alcohol) (Found : N, 8·75. $C_{13}H_9O_4N_2ClS$ requires N, 8·6%).

2 : 4-*Dinitro*-1 : 5-*diphenylthiobenzene*, needles, m. p. 253° (Found : N, 7·4. $C_{18}H_{12}O_4N_2S_2$ requires N, 7·3%), and 5-*chloro*-2 : 4-*dinitrodiphenyl sulphide*, needles, m. p. 108° (Found : N, 9·0. $C_{12}H_7O_4N_2ClS$ requires N, 9·0%), were similarly prepared by means of thiophenol.

2 : 4-*Dinitro*-1 : 5-*di*-p-*tolylsulphonylbenzene* (II).—(A) The dithioether (VII) was oxidised by heating with excess of hydrogen peroxide in acetic acid solution for 2 hours at 100°. (B) *p*-Toluenesulphinic acid (2 g.) and 1 : 5-dichloro-2 : 4-dinitrobenzene (1·5 g.) were refluxed in alcohol (30 c.c.) for 30 minutes. In each case the *product*, after crystallisation from acetic acid, melted at 228° (Found : S, 13·3. $C_{20}H_{16}O_8N_2S_2$ requires S, 13·45%). Treatment of its alcoholic dioxan solution as described under (VII, above) gave the dithioether (VII), m. p. and mixed m. p. 233°.

2 : 4-*Dinitro*-1 : 5-*diphenylsulphonylbenzene* (IV), m. p. 251°, was obtained by similar methods (Found : S, 14·5. $C_{18}H_{12}O_8N_2S_2$ requires S, 14·3%).

1 : 2 : 4 : 5-*Tetra*-p-*tolylsulphonylbenzene* (III).—1 : 5-Dichloro-2 : 4-dinitrobenzene (2 g.) in warm alcohol (30 c.c.) and sodium *p*-toluenesulphinate (6 g.) in hot water (18 c.c.) were mixed and refluxed for 1 hour. The precipitate which rapidly formed melted indefinitely at 279° and was similar to that produced when (II) was heated (1 hour) with the sulphinate in acetic acid. Each product was partially purified (m. p. 306°) by crystallisation from methyl ethyl ketone, but residual nitro-compounds were best removed by reduction with stannous chloride and concentrated hydrochloric acid (9 g. and 100 c.c. respectively per 1·5 g. of material) in acetone (300 c.c.), followed by treatment with 20% sodium hydroxide solution (150 c.c.) and extraction of the solid with acetone. After crystallisation from methyl ethyl ketone the *product*, m. p. 315°, was free from nitrogen (micro-Dumas) (Found : S, 18·1. $C_{34}H_{30}O_8S_4$ requires S, 18·4%).

1 : 2 : 4 : 5-*Tetraphenylsulphonylbenzene* (V) was prepared by refluxing (IV) in acetic acid–ethylene glycol (1 : 1) with sodium benzenesulphinate (5 mols.) for a few minutes, heating being stopped when colour began to be developed. On cooling, the *product* separated; it crystallised from methyl ethyl ketone in colourless needles (nitrogen-free), m. p. 305° (Found : S, 19·8. $C_{30}H_{22}O_8S_4$ requires S, 20·0%).

2 : 4-*Diamino*-1 : 5-*di*-p-*tolylsulphonylbenzene* (VI, X = NH_2).—(A) Either (II) or (III) in methyl alcohol (20 c.c. per 2 g.) was heated in a sealed tube at 150° with concentrated aqueous ammonia (3 c.c., *d* 0·88) for 3 hours; cream-coloured needles were deposited on cooling. These were washed with boiling acetone and were obtained colourless by crystallisation from ethylene glycol; m. p. 293°. (B) The same *compound* was obtained by reduction of (II) (2 g.) with stannous chloride (18 g.) and hydrochloric acid (20 c.c.) in alcohol (20 c.c.), followed by treatment with 20% sodium hydroxide solution (300 c.c.) and extraction of the solid with acetic acid (Found : N, 6·8. $C_{20}H_{20}O_4N_2S_2$ requires N, 6·7%).

2 : 4-*Dipiperidino*-1 : 5-*di*-p-*tolylsulphonylbenzene* (VI, X = NC_5H_{10}) was prepared by heating (II) or (III) with excess of piperidine for 2 minutes. The solution was cooled, water added, and the precipitated solid extracted with concentrated hydrochloric acid, from which the compound was reprecipitated by addition of water. The product formed yellow plates, m. p. 228° (from alcohol) (Found : N, 4·95. $C_{30}H_{36}O_4N_2S_2$ requires N, 5·0%).

2 : 4-*Dipiperidino*-1 : 5-*diphenylsulphonylbenzene*, m. p. 221°, was prepared from (IV) in the same way (Found : N, 5·45. $C_{28}H_{32}O_4N_2S_2$ requires N, 5·3%).

5-*Chloro*-2 : 4-*dinitro*-4′-*methyldiphenylsulphone* (IX) was prepared by oxidation of the sulphide with hydrogen peroxide in acetic acid; m. p. 198° (from acetic acid) (Found : N, 8·0. $C_{13}H_9O_6N_2ClS$ requires N, 7·9%). Treatment of an alcoholic dioxan solution of the compound with *p*-thiocresol (1 mol.) and 10% sodium hydroxide solution gave a mixture of mono- and di-thioethers (VIII and VII, separated as under VIII), whilst with thiophenol the corresponding phenyl derivatives were produced.

5-*Chloro*-2 : 4-*dinitrodiphenylsulphone*, m. p. 187°, was similarly prepared (Found : S, 9·4. $C_{12}H_7O_6N_2ClS$ requires S, 9·4%).

2 : 4-*Dinitro*-5-*piperidino*-4′-*methyldiphenylsulphone* (X) was obtained in felted orange-yellow needles, m. p. 180° (from alcohol), by refluxing an aqueous alcoholic solution of 5-chloro-2 : 4-dinitropiperidinobenzene (Le Fèvre and Turner, *loc. cit.*) and sodium *p*-toluenesulphinate. The same compound was formed by heating (IX) with excess of piperidine (Found : N, 10·3. $C_{18}H_{19}O_6N_3S$ requires N, 10·4%).

2 : 4-*Dinitro*-5-*piperidino*-4′-*methyldiphenyl sulphide* (XIII) was prepared by refluxing (VIII) in piperidine (1 hour) and also by treating (X) or (XII) in alcohol with *p*-thiocresol and sodium hydroxide in the usual way; it formed yellow plates, m. p. 192°, from alcoholic dioxan (Found : N, 11·2. $C_{18}H_{19}O_4N_3S$ requires N, 11·3%).

Compounds (IX), (VIII), and (XII) were each heated in acetic acid solution with *p*-toluene-

sulphinic acid (1 mol.). (IX) yielded 2 : 4-dinitro-1 : 5-di-*p*-tolylsulphonylbenzene (m. p. and mixed m. p.) and (VIII) and (XII) were recovered unchanged.

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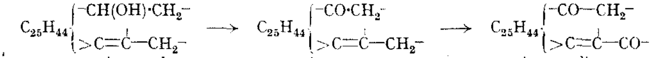
THE UNIVERSITY, GLASGOW. [*Received, November 25th,* 1936.]

45. *The Resinols. Part IV. The Structure of α-Amyrenol.**

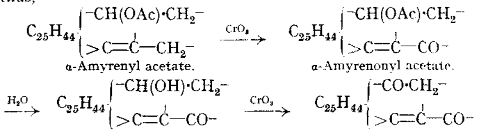
By F. S. SPRING and T. VICKERSTAFF.

OXIDATION of α-amyrenol or of α-amyrenone with chromic anhydride has been shown to give α-amyrenone oxide I, m. p. 193°, to which the formula $C_{30}H_{48}O_2$ has been ascribed. It is established that one of the oxygen atoms of α-amyrenone oxide I is present as a carbonyl group which originates in the secondary hydroxyl group of α-amyrenol (Spring and Vickerstaff, J., 1934, 650, 1859).

An analytical study of α-amyrenone oxide I and its allies has now established that its molecular formula is $C_{30}H_{46}O_2$ and not $C_{30}H_{48}O_2$: hence the formation of α-amyrenone oxide from α-amyrenone is consequent upon the oxidation of a methylene group in the α-position to the ethylenic linkage, to a carbonyl group; α-amyrenone oxide is therefore an α-amyrenedione and the oxidation of α-amyrenol proceeds according to the scheme:

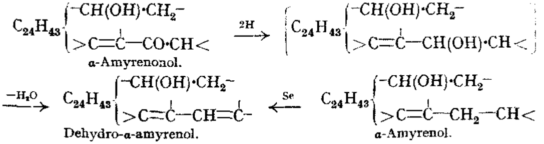


Similarly, α-amyrenol oxide (Spring and Vickerstaff, *loc., cit.*; Vesterberg, *Ber.*, 1891, **24**, 3836) has the molecular formula $C_{30}H_{48}O_2$ and not $C_{30}H_{50}O_2$. In addition to the secondary hydroxyl group of α-amyrenol, α-amyrenol oxide contains a carbonyl group introduced thus,



and is therefore to be designated α-amyrenonol. Dehydration of α-amyrenonol with phosphorus pentachloride gives a mixture of two unsaturated ketones, *α-amyradienones* I and II, a reaction which is paralleled by the dehydration of α-amyrenol to dextro-α-amyradiene and α-amyradiene (Vesterberg, *Ber.*, 1887, **20**, 1242; 1891, **24**, 3834).

The carbonyl group of α-amyrenonol is completely inactive towards the usual ketonic reagents; the presence of the group has been confirmed indirectly by reduction with sodium and amyl alcohol, whereby dehydro-α-amyrenol was obtained, identical with that prepared by Jacobs and Fleck (*J. Biol. Chem.*, 1930, **88**, 137) by the partial dehydrogenation of α-amyrenol with selenium; the formation of dehydro-α-amyrenol is represented by the scheme:

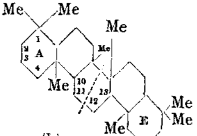


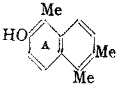
* In order to rationalise the nomenclature of the series, all derivatives of the amyrins will be referred to the unknown saturated hydrocarbons α- and β-amyranes; the naturally occurring monoethenoid alcohols will therefore be designated α- and β-amyrenols.

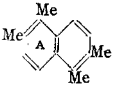
Final confirmation of the correctness of the molecular structure suggested for α-amyrenonol was obtained in the observation that it exhibits the typical ultra-violet absorption spectrum of an αβ-unsaturated ketone. The fact that both α-amyrenedione and α-amyrenonol fail to give colorations with tetranitromethane in chloroform (Spring and Vickerstaff, *loc. cit.*) is in harmony with previous experience of this reagent with αβ-unsaturated ketones (Werner, *Ber.*, 1909, **42**, 4324; Ostromisslensky, *J. pr. Chem.*, 1911, **84**, 489; Ruzicka, Huyser, Pfeiffer, and Seidel, *Annalen*, 1929, **471**, 21).

Hitherto there has been no satisfactory proof of the presence of an ethylenic linkage in α-amyrenol, the alcohol and its esters being completely resistant to catalytic hydrogenation. Again, whilst α-amyrenyl acetate is recovered unchanged after treatment with perbenzoic acid, we find that dehydro-α-amyrenyl acetate gives a monoxide, thus affording a proof that it contains one ethylenic linkage more than α-amyrenol. The recognition of α-amyrenonol as an αβ-unsaturated ketone affords a very necessary confirmation of the unsaturated nature of α-amyrenol, whilst the reduction of the ketone to dehydro-α-amyrenol defines this unsaturated centre as $>C{=}\overset{|}{C}{-}CH_2{-}CH<$.

Dehydrogenation of α-amyrenol with selenium gives a mixture, from which 1 : 2 : 7-trimethylnaphthalene (sapotalin), 1 : 2 : 5 : 6-tetramethylnaphthalene, 1 : 5 : 6-trimethyl-β-naphthol (II), and the hydrocarbon $C_{25}H_{20}$ (?), m. p. 306°, have been isolated; each of these products has previously been obtained by the dehydrogenation of the mixed α- and β-amyrenols (Ruzicka and Huyser, *Annalen*, 1929, **471**, 35; Ruzicka, Silbermann, and Pieth, *Helv. Chim. Acta*, 1932, **15**, 1285). The hydrocarbon $C_{25}H_{20}$ (?) is a picene homologue (Ruzicka, Hosli, and Ehmann, *Helv. Chim. Acta*, 1934, **17**, 442; Ruzicka and Mörgeli, *ibid.*, 1936, **19**, 377; Bernal and Crowfoot, J., 1935, 93), the formation of which proves that α-amyrenol has the hydropicene structure of oleanolic acid and hederagenin. A satisfactory representation of the carbon skeleton of the pentacyclic triterpenes that give the hydrocarbon $C_{25}H_{20}$ (?) on dehydrogenation is (I) (Spring, *J. Soc. Chem. Ind.*, 1936, **55**, 1050).


(I.)


(II.)


(III.)

The structure of α-amyrenol is to be derived from (I) by the introduction of a secondary hydroxyl group and one ethenoid linkage. The isolation of the naphthol (II) from the dehydrogenation products of α-amyrenol locates the secondary hydroxyl group of the latter at C_2; preliminary retropinacolinic rearrangement of the hydroxylated ring A satisfactorily interprets the formation of 1 : 2 : 5 : 6-tetramethylnaphthalene (III) (Ruzicka, Hofmann, and Schellenberg, *Helv. Chim. Acta*, 1936, **19**, 1391). Since the ethenoid linkage of α-amyrenol is present in the system $>C{=}\overset{|}{C}{-}CH_2{-}\overset{|}{C}H{-}$, it must be located at either $C_{10}-C_{11}$ or $C_{12}-C_{13}$. This decision is dependent upon the assumption that dehydro-α-amyrenol contains the same carbon skeleton as α-amyrenol.

Experimental.

α-Amyrenonol.—A more efficient method for the preparation of α-amyrenonol is oxidation of α-amyrenyl benzoate, and hydrolysis of the resulting *α-amyrenonyl benzoate*. A suspension of α-amyrenyl benzoate (4 g.) in boiling acetic acid (50 c.c.) was treated with a solution of chromic anhydride (2 g.) in 85% acetic acid (10 c.c.), added during 1 hour. After boiling for 1 hour, the solution was cooled and the solid separating was repeatedly crystallised from benzene–alcohol, from which *α-amyrenonyl benzoate* separated in colourless laminæ, m. p. 266° (Table I, 3). The benzoate (13 g.) in benzene (35 c.c.) was added to 12% alcoholic potassium hydroxide (150 c.c.), and the mixture heated under reflux for 20 hours. After dilution with water the mixture was

extracted with benzene. The dry benzene extract was concentrated, and crystallisation effected by the addition of ligroin (b. p. 40—60°). Recrystallisation of this solid gave α-amyrenonol in stout needles, m. p. 208°, showing no depression on admixture with the material prepared by the method of Vesterberg (*loc. cit.*) (Table I, 1). *Light absorption in alcohol* :* maxima, (*a*) 2500 A., log ε = 4·08; (*b*) 3150 A., log ε = 1·7.

TABLE I.

	% C.*			% H.*		
	Found.	A.	B.	Found.	A.	B.
1. α-Amyrenonol	82·0	81·75	81·4	11·1	11·0	11·4
,,	82·2			11·1		
2. α-Amyrenonyl acetate	79·4	79·6	79·3	10·6	10·5	10·8
3. α-Amyrenonyl benzoate	81·5	81·6	81·3	9·4	9·6	10·0
4. α-Amyrenedione	82·5	82·1	81·75	10·4	10·6	11·0
5. α-Amyradienone I	85·2	85·2	84·8	11·15	11·0	11·4
6. α-Amyradienone II	85·3	85·2	84·8	11·1	11·0	11·4

* The theoretical values under A and B are calculated from the formulæ $C_{30}H_{46}O_2$ and $C_{30}H_{50}O_2$ respectively for α-amyrenonol.

α-Amyradienones I and II.—Finely powdered α-amyrenonol (10 g.) was added during 1 hour to a suspension of phosphorus pentachloride (6·4 g.) in ligroin (b. p. 40—60°; 60 c.c.), and after 3 hours the mixture was boiled under reflux for 30 minutes. The solution was washed with water and dried and the residue obtained after removal of the solvent was crystallised from alcohol, from which *α-amyradienone I* separated in needles, m. p. 197°, $[\alpha]_D^{20°}$ + 166° (*l* = 1, *c* = 0·042 in chloroform) (Table I, 5). The alcoholic mother-liquor from the dienone I on long standing deposited prisms containing a trace of chlorine which could not be removed by crystallisation. Removal of halogen was effected by warming with alcoholic sodium ethoxide and repeated crystallisation then gave *α-amyradienone II* in prisms, m. p. 156°, $[\alpha]_D^{20°}$ + 153° (*l* = 1, *c* = 0·088 in chloroform) (Table I, 6). If the amyrenonol is added in one portion to the phosphorus pentachloride suspension in ligroin, and the mixture kept overnight, α-amyradienone II is obtained as sole product.

Dehydro-α-amyrenol.—A solution of α-amyrenonol (5 g.) in boiling amyl alcohol (150 c.c.) was treated with sodium (10 g.), added as quickly as the reaction would permit. The mixture was boiled for 1 hour, cooled, and the amyl alcohol removed by distillation in steam. The separated solid was isolated by means of ether and repeatedly crystallised from benzene, from which dehydro-α-amyrenol separated in feathery needles, m. p. 160°. It was characterised by the preparation of its benzoate, m. p. 174° (Found: C, 83·9; H, 9·6. Calc. for $C_{37}H_{52}O_2$: C, 84·0; H, 9·9%), by oxidation to dehydro-α-amyrenone, m. p. 135—137° (Found: C, 85·1; H, 11·15. Calc. for $C_{30}H_{46}O$: C, 85·2; H, 11·0%), and by the preparation of the oxime of the latter, m. p. 236°. Jacobs and Fleck (*loc. cit.*) give m. p. 171—172° for dehydro-α-amyrenyl benzoate, m. p. 133—134° for dehydro-α-amyrenone, and m. p. 235° for the oxime of the ketone. The *acetate* was prepared by refluxing dehydro-α-amyrenol with acetic anhydride (50 c.c.) and potassium acetate (1 g.) for 1 hour. The solid separating from the cooled solution was recrystallised from acetic acid, from which the acetate separated in long needles, m. p. 170° (Found: C, 82·2; H, 10·9. $C_{32}H_{50}O_2$ requires C, 82·3; H, 10·8%).

Dehydro-α-amyrenyl Acetate Oxide.—Dehydro-α-amyrenyl acetate (0·8 g.) was treated with a chloroform solution of perbenzoic acid (0·6 *N*; 25 c.c.) and set aside for 14 days. The chloroform solution was washed with aqueous sodium carbonate, dried (sodium sulphate), and the solvent removed; repeated crystallisation of the residue from methyl alcohol gave the *oxide* in needles, m. p. 192° (Found: C, 80·0; H, 10·6. $C_{32}H_{50}O_3$ requires C, 79·6; H, 10·5%).

Dehydrogenation of α-Amyrenol.—An intimate mixture of α-amyrenol (90 g.) and selenium (130 g.) was heated under an air-condenser by means of a bath of sodium nitrate–sodium nitrite. The first vigorous reaction having abated, the bath temperature was raised to and maintained at 350° for 40 hours. After cooling, the reaction mixture was extracted with ether (Soxhlet), the extract filtered, and the solvent removed. Distillation of the residual oil gave the following fractions: (*a*) 80—120°/7 mm., mobile yellow oil (1 g.); (*b*) 120—150°/5 mm., yellow oil (5 g.); (*c*) 150—210°/4 mm., brown viscous oil (4 g.); (*d*) 200—270°/1 mm., red resin (5 g.); (*e*) 300°/0·1 mm., red resin (7 g.). Fraction (*b*) was treated with an equal weight of picric acid in alcohol. The separated picrate mixture was washed with alcohol, and the hydrocarbon regenerated by solution in ether, followed by washing with dilute aqueous ammonia. Removal of the solvent

* The authors' thanks are due to Mr M. S. El. Ridi for these measurements.

from the dried ethereal solution gave the hydrocarbon mixture as a viscous yellow oil, which, on standing at 0° for 14 days, partly solidified. The crystalline hydrocarbon, m. p. 110°, was freed from oil by washing with light petroleum and treated with an equal weight of picric acid in alcohol. The picrate separated in red needles, which attained the constant m. p. 156° after repeated crystallisation (Ruzicka, Ehmann, and Mörgeli, *Helv. Chim. Acta*, 1933, **16**, 314, give m. p. 154—154·5° for the picrate of synthetic 1 : 2 : 5 : 6-tetramethylnaphthalene). One half of the oily hydrocarbon obtained by removal of the solvent from the light petroleum washings of tetramethylnaphthalene was treated with a solution of picric acid in alcohol. Recrystallisation of the picrate from alcohol gave 1 : 2 : 7-trimethylnaphthalene picrate in orange-red needles, m. p. 129·5—130° (Ruzicka and Ehmann, *Helv. Chim. Acta*, 1932, **15**, 140, give m. p. 129° for the picrate of synthetic 1 : 2 : 7-trimethylnaphthalene) (Found: C, 57·3; H, 4·5. Calc. for $C_{19}H_{17}O_7N_3$: C, 57·1; H, 4·5%). The remaining portion of the hydrocarbon was converted into its styphnate, which had the constant m. p. 156° (Ruzicka and Ehmann, *loc. cit.*, give m. p. 156° for the styphnate of synthetic 1 : 2 : 7-trimethylnaphthalene).

Fraction (*c*) was redistilled at 75°/10^{-3} mm., a yellow oil collecting in the receiver which partly solidified on cooling. After trituration with light petroleum, the solid was repeatedly crystallised from the same solvent, from which 1 : 5 : 6-trimethyl-β-naphthol separated in colourless needles, m. p. 155°, completely soluble in dilute potassium hydroxide solution to a blue fluorescing solution. For analysis the naphthol was sublimed, without, however, raising the m. p. (Found: C, 83·75; H, 7·8. Calc. for $C_{13}H_{14}O$: C, 83·8; H, 7·6%).

A solution of fraction (*e*) in boiling butyl alcohol was allowed to cool slowly, the amorphous yellow solid separating being collected and washed with the same solvent. Sublimation of this solid at 200—240°/10^{-3} mm., followed by repeated crystallisation of the sublimate from pyridine–butyl alcohol, gave trimethylpicene(?) in needles, m. p. 306° (Found: C, 93·7; H, 6·3. Calc. for $C_{25}H_{20}$: C, 93·7; H, 6·3%).

THE UNIVERSITY, MANCHESTER. [*Received, December 1st*, 1936.]

46. *The Reaction between Sodium Iodide and Toluenesulphonyl Derivatives of Glucofuranose.*

By D. J. BELL, E. FRIEDMANN, and S. WILLIAMSON.

OLDHAM and RUTHERFORD (*J. Amer. Chem. Soc.*, 1932, **54**, 366) have shown that arylsulphonyl groups occupying position 6 in the glucopyranose chain are quantitatively replaced by iodine after two hours' heating at 100° with sodium iodide in acetone: under these conditions, groups in positions other than 6 are unaffected. As a means of identifying and eliminating 6-arylsulphonyl groups, this reaction has been employed by Oldham and Rutherford (*ibid.*, p. 1086), by Bell (J., 1934, 1177; 1936, 186), and, in a modified form, by Hess and Pfleger (*Annalen*, 1933, **507**, 48), Hess and Littman (*Ber.*, 1934, **67**, 465), and Hess and Eveking (*ibid.*, p. 1908).

Apart from reporting no reaction with 3-*p*-toluenesulphonyl diacetone glucose and with amorphous 5-*p*-toluenesulphonyl 2 : 3 : 6-trimethyl γ-methylglucoside, Oldham and Rutherford made no systematic examination in the furanose series. This we have now carried out, using crystalline glucofuranose derivatives, two of which are described for the first time. Treated according to Oldham and Rutherford, the following substances were recovered unchanged: 2-p-*toluenesulphonyl* 3 : 5 : 6-*tribenzoyl* β-*methylglucofuranoside*, 3-*p*-toluenesulphonyl diacetone glucose (Freudenberg and Ivers, *Ber.*, 1922, **55**, 929), and 5-*p*-toluenesulphonyl 6-acetyl monoacetone glucose (Ohle, Euler, and Lichtenstein, *Ber.*, 1929, **62**, 2885). Reaction ensued when the sulphonyl group occupied position 6, and, depending upon whether or not the adjacent 5-hydroxyl group was substituted, the products formed were of completely different type. 6-*p*-Toluenesulphonyl monoacetone glucose (Ohle and Dickhäuser, *Ber.*, 1928, **58**, 2593) yielded material free from iodine and sulphur, and with an unsaturated linkage. Further examination was not made, but it is suggested that the most probable product would be a derivative of 5 : 6-glucoseen. On the other hand, 6-p-*toluenesulphonyl* 3 : 5-*benzylidene monoacetone glucose* reacted smoothly to give the corresponding 6-*iodide* in good yield. The latter on heating in acetonitrile with silver *p*-toluenesulphonate re-formed the 6-*p*-toluenesulphonate.

Attempts to prepare, in the following manner, 5-toluenesulphonyl 3-methyl monoacetone glucose repeatedly ended in failure. 3-Methyl monoacetone glucose with *p*-toluenesulphonyl chloride in pyridine gave an amorphous product, which, with sodium iodide in acetone, gave largely sulphur-free derivatives together with a certain amount of a crystalline substance, tentatively described as *6-chloro 5-p-toluenesulphonyl 3-methyl monoacetone glucose.* This substance was always formed when 3-methyl monoacetone glucose was toluenesulphonated, and could be isolated from the crude product without employing the sodium iodide reaction. It appears to be analogous to 6-chloro 2 : 3-di-*p*-toluenesulphonyl 4-acetyl α-methylglucoside (Littman and Hess, *Ber.*, 1934, **67**, 519) and resembles it in its stability. Neither the sulphonyl radicals nor the chlorine was affected by sodium iodide in acetone, nor was the chlorine replaced by toluenesulphonyl on boiling with the silver salt in acetonitrile.

Thus it appears that, in glucofuranose derivatives, as in the corresponding pyranose series, toluenesulphonyl groups occupying position 6 are alone reactive towards sodium iodide, with replacement by iodine, but only if the hydroxyl group of position 5 is adequately protected against the production of an unsaturated linkage.

EXPERIMENTAL.

Solvents were evaporated under reduced pressure, below 50°, polarimetric observations were made in chloroform solution in a 2 dm. tube, and substances were recrystallised to constant m. p. Heating with sodium iodide was carried out exactly as described by Oldham and Rutherford.

2-p-*Toluenesulphonyl* 3 : 5 : 6-*Tribenzoyl* β-*Methylglucofuranoside.*—3·9 G. of the crystalline 3 : 5 : 6-tribenzoyl glucofuranose–carbon tetrachloride addition compound of Fischer and Rund (*Ber.*, 1916, **49**, 88) were treated with 3 g. (3 mols.) of toluenesulphonyl chloride in pyridine for 24 hours. The crude tarry product was precipitated by the addition of water, well washed, dissolved in benzene and ether, and filtered through norit. The residue, after evaporation of the solvents, was dissolved in 25 ml. of acetic acid containing 50% of its weight of hydrobromic acid and kept for 6 hours. Benzene was added and the acetic and hydrobromic acids were washed out, first with water, and then with potassium bicarbonate solution. After dehydration over calcium chloride the benzene solution was concentrated to a thick syrup, which was mixed with methyl alcohol (10 vols.), shaken with silver carbonate for 2 hours, and kept over-night. Evaporation of the solvent yielded 1 g. of crystals. Recrystallised from ethyl alcohol, the *substance* formed fine needles, m. p. 125—127°, $[\alpha]_D^{20°}$ − 61·9° (*c*, 4·5) (Found : S, 5·2; OMe, 4·5. $C_{35}H_{32}O_{11}S$ requires S, 4·8; OMe, 4·7%). The β-configuration is assigned on account of the method of synthesis and the strongly negative rotation.

6-p-*Toluenesulphonyl* 3 : 5-*Benzylidene Monoacetone Glucose.*—4 G. of 3 : 5-benzylidene monoacetone glucose (Brigl and Gruner, *Ber.*, 1932, **65**, 1428), dissolved in the minimum of pyridine, were treated with 1·5 mols. of finely powdered *p*-toluenesulphonyl chloride for 24 hours at room temperature. Water was then added and the crystals were separated, washed with water, and recrystallised from ethyl alcohol, forming needles (4 g.), m. p. 118°, $[\alpha]_D^{20°}$ + 14·2° (*c*, 5) (Found : S, 6·9. $C_{23}H_{26}O_8S$ requires S, 6·9%).

6-*Iodo* 3 : 5-*Benzylidene Monoacetone Glucose.*—2 G. of the above toluenesulphonate were treated according to Oldham and Rutherford. The *product* (needles, 1·5 g.), recrystallised from ethyl alcohol, had m. p. 137°, $[\alpha]_D^{20°}$ + 17·7° (*c*, 9·7) (Found : I, 12·9. $C_{16}H_{19}O_5I$ requires I, 30·3%). The iodo-compound, heated with silver toluenesulphonate in acetonitrile in a sealed tube at 100° for 12 hours, regenerated the toluenesulphonate, m. p. 118° alone or mixed with authentic material.

Chloro p-*Toluenesulphonyl* 3-*Methyl Monoacetone Glucose.*—20 G. of 3-methyl monoacetone glucose were treated with 82 g. of *p*-toluenesulphonyl chloride, dissolved in dry pyridine, for 5 days at 30°. After washing in benzene solution, the crude product was isolated as a dark-coloured glass which could not be crystallised. After extraction with much boiling ligroin, a dark residue remained undissolved. On allowing the ligroin to evaporate at room temperature, crystals were deposited : recrystallised from ethyl alcohol and acetone, 5 g. of needles were obtained, m. p. 143°, $[\alpha]_D^{15°}$ − 46·6° (*c*, 7) (Found : OMe, 7·7; S, 7·5; Cl, 8·2. $C_{17}H_{23}O_7SCl$ requires OMe, 7·6; S, 7·8; Cl, 8·7%).

THE BIOCHEMICAL LABORATORY, CAMBRIDGE. [*Received, November 24th,* 1936.]

47. *Hydroxyanthraquinones. Part II.* 1 : 2 : 5 : 6- *and* 1 : 4 : 5 : 8-*Tetrahydroxyanthraquinones.*

By Philip Guy Marshall.

Following the work reported in Part I (J., 1931, 3206), it was considered of interest to investigate the sulphonation of anthrarufin and the production of the corresponding hydroxyanthraquinone obtained by alkali fusion of the sodium salt.

Whilst quinizarin gives a quantitative yield of the sodium 2-sulphonate on boiling with aqueous sodium sulphite in the presence of copper oxide (*loc. cit.*), alizarin does not react when similarly treated and only an infinitesimal amount of a water-soluble product (? sulphonate) is formed from anthrarufin even after boiling for 24 hours under the above conditions. Anthrarufin has been reported to yield the disulphonic acid on heating with 4 parts of 20% oleum at 100—120° until completely soluble in water (Baeyer & Co., *Zentr.*, 1898, I, 1255), but no further details are given. In the present work the disulphonic acid was produced in good yield by a brief heating at 140—150° with 3—4 parts of 20% oleum. It has also been reported (Baeyer & Co., D.R.P. 103,988) that the sodium salt of the sulphonic acid yields, on alkali fusion at 200—280°, 1 : 2 : 5 : 6-tetrahydroxyanthraquinone; no further details of the conditions or yield are given. The author found that the reaction does not proceed to any appreciable extent at 200—230°, and at 280° decomposition is so extensive that very little of the desired product can be isolated. It is possible, however, to obtain a yield of 70—75% by proper control of the conditions. The 1 : 2 : 5 : 6-tetrahydroxyanthraquinone obtained can be sulphonated by heating with 3—4 parts of 20% oleum at 120—130°; a yield of over 90% of the sodium salt of the disulphonic acid is obtained. Repeated attempts to produce the corresponding hexahydroxyanthraquinone by alkali fusion under various conditions, with or without the addition of sodium chlorate, were unsuccessful.

It seemed more likely that *1 : 4 : 5 : 8-tetrahydroxyanthraquinone* would behave similarly to quinizarin on boiling with sodium sulphite in the presence of copper oxide. The preparation of this substance was therefore undertaken. It was not found possible to obtain it by diazotisation of diaminoanthrarufin in concentrated sulphuric acid solution, followed by dilution and boiling in the usual way; the chocolate-brown product was almost insoluble in concentrated sulphuric acid, aqueous sodium hydroxide or nitrobenzene. The leuco-compound of 1 : 4 : 5 : 8-tetrahydroxyanthraquinone was, however, obtained in good yield by boiling diaminoanthrarufin in alkaline solution with sodium hyposulphite, and this can be quantitatively oxidised by a brief boiling in nitrobenzene solution, from which the anthraquinone derivative crystallises on cooling. It cannot be sulphonated by boiling with aqueous sodium sulphite in the presence of copper oxide.

Experimental.

Anthrarufindisulphonic Acid.—50 G. of anthrarufin and 90 c.c. of 20% oleum were heated at 120° for 3 hours. The cooled melt was poured into 2½ l. of water, the filtered, dark orange-brown solution warmed to 60°, and the sodium salt of the disulphonic acid precipitated by addition of sodium chloride. The product was dissolved in 5 l. of hot water, 50 g. of sodium chloride added, and the sodium salt allowed to crystallise. Yield, 70 g.

1 : 2 : 5 : 6-*Tetrahydroxyanthraquinone.*—40 G. of sodium hydroxide were heated in a nickel crucible with a little water and 1 g. of sodium chlorate until molten, and 10 g. of disodium anthrarufindisulphonate were gradually stirred in. The temperature was then raised to 260—270° for 15 minutes with continuous stirring. After cooling, the mass was extracted with 1 l. of hot water and acidified with hydrochloric acid. The orange-brown precipitate was collected, washed with a large volume of hot water, and dried. Yield, 4·6 g. (75%). The product crystallises in pure condition from pyridine in orange-red needles, m. p. > 300° (Found: C, 62·3; H, 3·0. Calc. for $C_{14}H_8O_6$: C, 61·8; H, 2·9%); it dissolves in alkalis with a crimson, and in concentrated sulphuric acid with a purple colour. The *tetra-acetyl* derivative occurs in yellow needles, m. p. 260—275° (decomp.) (Found: C, 59·2; H, 3·6. $C_{22}H_{16}O_{10}$ requires C, 60·0; H, 3·6%).

Leuco-1 : 4 : 5 : 8-*tetrahydroxyanthraquinone.*—A mixture of 40 g. of diaminoanthrarufin, 80 g. of sodium hydroxide, and 2 l. of water was heated to boiling, 80 g. of sodium hyposulphite

added gradually, and boiling continued for 1 hour until ammonia was no longer evolved, the final volume being 1000—1500 c.c. When cold, the sodium salt of the leuco-compound was filtered off, washed with water, and dried (dark needles with bronze-green reflex). Yield, 48 g. (80%). The free leuco-compound was obtained in theoretical yield by suspending the sodium salt in hot water and acidifying with hydrochloric acid. It crystallised from glacial acetic acid in bronze needles, m. p. > 290° (decomp.) (acetyl derivative m. p. 235—240° decomp.).

1 : 4 : 5 : 8-*Tetrahydroxyanthraquinone* was obtained by heating 32 g. of the leuco-compound with 250 c.c. of nitrobenzene almost to boiling; the orange-brown solution rapidly became crimson, and the heat of the reaction caused the mixture to boil gently for a few minutes. Water was evolved and the solution was boiled for a brief period to expel it. After 12 hours the solution became blue-violet, probably owing to traces of unchanged diaminoanthrarufin. The *product*, which occurred as dark brown to black shining needles, was filtered off and washed with nitrobenzene and a large volume of ether. The yield was almost theoretical; m. p. > 300° (Found : C, 61·5; H, 3·0. $C_{14}H_8O_6$ requires C, 61·8; H, 2·9%). The product dissolved in glacial acetic acid with a crimson colour (cf. diaminoanthrarufin, which yields a blue solution). The *acetyl* derivative, prepared in the usual way, crystallised from glacial acetic acid in brownish-yellow needles, m. p. > 258° (decomp.) (Found : C, 60·1; H, 3·5. $C_{22}H_{16}O_{10}$ requires C, 60·0; H, 3·6%).

The author thanks the Chemical Society for a grant, Messrs. Scottish Dyes Ltd. for gifts of anthrarufin and diaminoanthrarufin, and The British Drug Houses Ltd. and Dr. H. G. Rule for facilities in carrying out the work.

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48. *The Action of Selenium on Compounds containing Quaternary Carbon Atoms.*

By GEORGE R. CLEMO and HAYDN G. DICKENSON.

As a corollary to the work on the dehydrogenation of compounds containing angular methyl groups (J., 1935, 735) it was of particular interest to examine the action of selenium at high temperatures (280—360°) on compounds containing quaternary carbon atoms.

The best-authenticated apparent exception to the useful head-to-tail isoprene polymerisation rule up to and including the diterpenes is abietic acid. Even in this case there is dispute as to whether this acid itself is ever a primary product, being ordinarily obtained from lævopimaric and *pro*abietic acids by treatment with acetic acid. If instead of the *iso*propyl substituent postulated from selenium degradation and other evidence at position 7 in abietic acid (I), the primary acids have either *gem**-methylethyl or -methylvinyl substituents attached, the rule holds as far as the diterpenes. It may be argued that, as the primary acids and also abietic acid condense with maleic anhydride, they have conjugated double bonds in ring (III) the possibility of a vinyl group at position 7 thus being ruled out, but such a condensation is not final proof of conjugation (compare Ruzicka, *Helv. Chim. Acta*, 1935, **18**, 219).

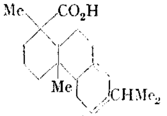
According to Kraft (*Annalen*, 1936, **524**, 1) the action of ozone on lævopimaric acid gives no formaldehyde, and although Ruzicka (*Helv. Chim. Acta*, 1925, **8**, 637) examined the action of ozone on abietic acid and its methyl ester, no mention is made of the production of formaldehyde. Under the conditions used by Clemo and Macdonald (J., 1935, 1294) abietic acid gives formaldehyde, but in amount insufficient to make certain of the presence of the $:CH_2$ group; and no lævopimaric acid is available for trial.

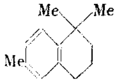
In the tetralin series, 1 : 1 : 6-trimethyltetralin (II) has been dehydrogenated by Ruzicka and Rudolph (*Helv. Chim. Acta*, 1927, **10**, 915), using sulphur, and by ourselves (*loc. cit.*), using selenium. In each case it was smoothly converted into 1 : 6-dimethylnaphthalene.

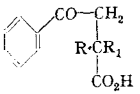
It was therefore decided to study in the first instance the dehydrogenation of 2 : 2-dialkyltetralins to test whether a *gem*-methylethyl group lost one of these groups or was

* The term *gem* is strictly applicable only to two like groups attached to the same atom, but its use here is extended to include two unlike groups.

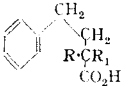
converted into an *iso*propyl group during the process of selenium dehydrogenation. An αα-dialkylsuccinic anhydride was condensed with benzene in the presence of aluminium chloride, and the resulting *β-benzoyl-αα-dialkylpropionic acid* (III) reduced to the corresponding *benzylpropionic acid* (IV). Ring closure and reduction gave the dialkyltetralin (V).

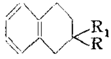

(I.)

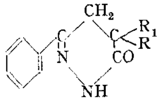

(II.)


(III.)

In this manner 2 : *2-dimethyl-* and *2-methyl-2-ethyl-tetralins* were synthesised. By analogy with the condensation of α-methylsuccinic anhydride and benzene (Oppenheim, *Ber.*, 1901, **34**, 4227; Meyer and Stamm, *ibid.*, 1923, **56**, 1424) the condensations would be expected to yield the αα-dialkyl acids (III) in preference to the ββ-dialkyl compounds. This is supported by the fact that, though the keto-acids (III) condense readily with hydrazine to give 6-*keto-3-phenyl-5 : 5-dialkyltetrahydropyridazines* (VI), the *tetralones* produced by ring closure of the acids (IV) would not react with hydrazine, hydroxylamine or semicarbazide, owing presumably to the blocking of the keto-group by the two adjacent alkyl groups.


(IV.)


(V.)


(VI.)

The dimethyl- and the methylethyl-tetralin (V; R = Me, R_1 = Me or Et) were obtained as colourless stable oils, but attempts to dehydrogenate them failed, prolonged treatment with selenium at 280—360° being without effect. This result is, at present, unexplained. That it is not due solely to the volatility of the hydrocarbon is clear, as both these compounds and 1 : 1 : 6-trimethyltetralin (II) have boiling points of the same order (*ca.* 130°/30 mm.). The above results give another instance of anomalous behaviour in selenium dehydrogenation and further investigation on these lines may serve to shed light on the mechanism of the reaction.

Experimental.

2 : *2-Dimethyltetralin* (V; R and R_1 = Me).—*β-Benzoyl-αα-dimethylpropionic acid* (III; R and R_1 = Me). αα-Dimethylsuccinic anhydride (6·2 g.) (Higson and Thorpe, J., 1906, **89**, 1465) was added slowly to powdered aluminium chloride (13 g.) in dry benzene (30 c.c.), the reaction being controlled by cooling and, after 1 hour, completed on the water-bath (1—2 hours). The mixture was poured into ice-cold 5% hydrochloric acid, the excess of benzene removed on the water-bath under reduced pressure, and, when cold, the solid product filtered off. The *keto-acid* obtained was practically pure and crystallised from hot alcohol in prisms, m. p. 173° (Found: C, 69·9; H, 6·95. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%).

6-*Keto-3-phenyl-5 : 5-dimethyltetrahydropyridazine* (VI, R and R_1 = Me), prepared by heating the above keto-acid with half its weight of hydrazine hydrate on the water-bath for 1 hour, was washed with water and recrystallised from hot alcohol, forming felty colourless needles, m. p. 167—168° (Found: C, 71·6; H, 7·1. $C_{12}H_{14}ON_2$ requires C, 71·3; H, 6·9%).

β-Benzyl-αα-dimethylpropionic acid (IV, R and R_1 = Me). The above keto-acid (10 g.) was refluxed with amalgamated zinc (50 g.) and concentrated hydrochloric acid (10 c.c.) for 15 hours, the *product* extracted with ether, dried, and filtered from high-melting by-products, and the solvent removed. The residue was distilled; it solidified instantly in the receiver and on recrystallisation from light petroleum formed fine needles (6 g.), m. p. 97°, b. p. 140—150°/0·2 mm. (Found: C, 74·7; H, 8·3. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·3%).

2 : *2-Dimethyl-1-tetralone*.—The above acid (5 g.) was covered with 80% sulphuric acid, kept overnight, and then heated for ½ hour on the water-bath, care being taken that no evolution of

sulphur dioxide occurred. The red solution was diluted with water and extracted with ether, and the extract washed with bicarbonate solution until neutral. It was then dried and distilled, giving the pure *ketone* (1·9 g.), b. p. 137°/15 mm. (Found : C, 82·4; H, 8·2. $C_{12}H_{14}O$ requires C, 82·7; H, 8·0%).

The ketone (1·5 g.) was refluxed with amalgamated zinc (15 g.) and concentrated hydrochloric acid (7 c.c.) for 12 hours, more acid (3 c.c.) then added, and refluxing continued for 3—4 hours. The product was extracted with ether and dried, the solvent removed, and the residue distilled. The pure 2 : 2-*dimethyltetralin* was redistilled over sodium and obtained as a colourless fragrant oil (0·9 g.), b. p. 104°/12 mm. (Found : C, 89·8; H, 9·7. $C_{12}H_{16}$ requires C, 90·0; H, 10·0%).

Attempted Dehydrogenation of 2 : 2-*Dimethyltetralin*.—The hydrocarbon (0·9 g.) in a 3 c.c. flask with a sealed-on air-condenser was refluxed with selenium (2 g.) for 15 hours at 280°. The heating was then continued at 300—320° for 12 hours and at 340—360° for a further 10 hours. The product was extracted with chloroform and filtered, the solvent removed, and the residue taken up with light petroleum. It was again filtered from precipitated selenium (charcoal) and refluxed for 2 hours over sodium, the solvent removed, and the residue distilled. It consisted entirely of unchanged material, b. p. 104—106°/12 mm. (Found : C, 89·8; H, 10·0%).

2-*Methyl*-2-*ethyltetralin* (V; R = Me, R_1 = Et).—β-*Benzoyl*-α-*methyl*-α-*ethylpropionic acid* (III; R = Me, R_1 = Et), prepared from α-methyl-α-ethylsuccinic anhydride (Higson and Thorpe, J., 1906, **89**, 1455) (4·8 g.) and aluminium chloride (7·2 g.) in benzene (18 c.c.) as in the case of the dimethyl compound, crystallised from alcohol in prisms, m. p. 94—95° (Found : C, 70·75; H, 7·2. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%).

6-*Hydroxy*-3-*phenyl*-5-*methyl*-5-*ethyltetrahydropyridazine* (VI; R = Me, R_1 = Et), prepared in a similar manner to the dimethyl compound (above), crystallised from petroleum (b. p. 80—100°) in stout needles or from dilute alcohol in prisms, m. p. 108° (Found : C, 72·1; H, 7·6. $C_{13}H_{16}ON_2$ requires C, 72·2; H, 7·4%).

β-*Benzyl*-α-*methyl*-α-*ethylpropionic acid* (IV; R = Me, R_1 = Et), prepared from the above keto-acid by reduction in the same manner as the dimethyl keto-acid (above), was distilled and then recrystallised from light petroleum, forming needles, m. p. 63° (Found : C, 75·9; H, 8·6. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%).

2-*Methyl*-2-*ethyl*-1-*tetralone* was obtained in the same way as the dimethyl compound. It was isolated as a colourless oil, b. p. 140°/13 mm. (Found : C, 83·0; H, 8·5. $C_{13}H_{16}O$ requires C, 83·0; H, 8·5%), and on reduction gave 2-*methyl*-2-*ethyltetralin* (V; R = Me, R_1 = Et), which was obtained as a colourless oil, b. p. 118°/20 mm. (Found : C, 89·9; H, 10·2. $C_{13}H_{18}$ requires C, 89·6; H, 10·4%).

Attempted Dehydrogenation of 2-*Methyl*-2-*ethyltetralin*.—The hydrocarbon (0·9 g.) was refluxed with selenium as before, for, in all, 48 hours at 280—360°. The product was extracted with light petroleum (b. p. 60—80°) and refluxed with sodium for ½ hour on the water-bath, and the solvent removed, yielding 0·62 g. of a colourless oil. It was distilled into three fractions : 78°/0·1 mm. (0·12 g.); 80—82°/0·1 mm. (0·36 g.); 82°/0·1 mm. (0·11 g.). None of these fractions yielded a picrate and the highest fraction gave the following analysis (Found : C, 90·3; H, 10·1. $C_{13}H_{18}$ requires C, 89·6; H, 10·4%. $C_{13}H_{16}$ requires C, 90·7; H, 9·3%).

Our thanks are due to the Chemical Society for a grant, to Mr. O. Telfer for the micro-analyses, and one of us (H. G. D.) is indebted to the Council of Armstrong College for a Scholarship.

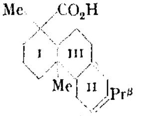
UNIVERSITY OF DURHAM, ARMSTRONG COLLEGE,
NEWCASTLE UPON TYNE. [*Received, December 1st*, 1936.]

49. *Studies in the Resin Acid Series. Part I. The Synthesis of Vocke's Unsaturated Acid*, $C_{10}H_{14}O_4$.

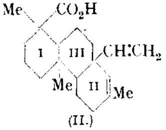
By H. N. RYDON.

ALTHOUGH the dehydrogenation of abietic acid (I) and dextropimaric acid (II) to retene and pimanthrene respectively and the synthesis of these hydrocarbons (for references, see Fieser, " Chemistry of Natural Products related to Phenanthrene," 1936) have conclusively established the basic structure of these resin acids, the method is incapable of affording definite evidence as to the position of those groups that are eliminated during dehydrogenation.

Direct synthetic evidence for the position of the carboxyl group and the methyl group in ring I is therefore lacking. The most suitable derivatives for the synthetic attack of this problem are the acids, $C_{11}H_{16}O_6$ and $C_{12}H_{18}O_6$, obtained by various workers by the oxida-



(I.)



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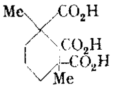

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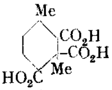
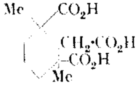


(IIIa.)

tion of abietic acid (Ruzicka, Meyer, and Pfeiffer, *Helv. Chim. Acta*, 1925, **8**, 637; Levy, *Ber.*, 1929, **62**, 2497; Ruzicka, Goldberg, Huyser, and Seidel, *Helv. Chim. Acta*, 1931, **14**, 545) and of dextropimaric acid (Ruzicka, de Graaff, Goldberg, and Frank, *Helv. Chim. Acta*, 1932, **15**, 915). Vocke (*Annalen*, 1932, **497**, 247) obtained from the C_{11} acid an unsaturated acid, $C_{10}H_{14}O_4$, and an isomeric lactonic acid; these he considered to have the structures (V) and (VI) respectively, leading to (III) and (IV) for the C_{11} and the C_{12} acid and finally to



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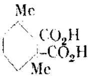

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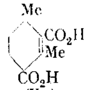
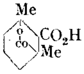


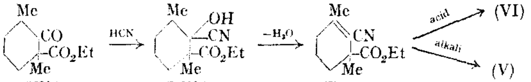
(Va.)



(VI.)

(I) and (II) for the parent resin acids, in so far as the arrangement of groups in ring I is concerned. The alternative structure (V*a*) for the unsaturated acid, leading to (III*a*) for the C_{11} acid, was not, however, completely excluded by the experimental evidence. Only synthesis could afford a final solution of the problem.

The acids (V) and (VI) have now been synthesised by the reactions



(VII.) (VIII.) (IX.)

and found to be identical with Vocke's two compounds. Only one of the possible stereoisomeric cyanohydrins (VIII) appears to be produced from the keto-ester (VII) by the action of hydrogen cyanide; this has the remarkably high m. p. of 75° and may be distilled in steam without decomposition.

It is therefore to be concluded that the C_{11} acid has the structure (III), the alternative structure (III*a*) being ruled out by the synthetic evidence. This affords the first direct synthetic evidence for the orientation of the substituents in ring I of abietic and dextropimaric acids. Final proof of this point rests with the synthesis of the C_{11} and the C_{12} acid; experiments with this end in view are in hand.

EXPERIMENTAL.

(All analyses are micro-analyses by Dr. G. Weiler, Oxford.)

Ethyl 2 : 6-dimethyl*cyclo*hexanone-2-carboxylate (VII), b. p. 92—94°/2·5 mm., was prepared in 78% yield by the methylation of the sodio-derivative of ethyl 2-methyl*cyclo*hexanone-6-carboxylate (Ruzicka, Koolhaas, and Wind, *Helv. Chim. Acta*, 1931, **14**, 1163) in petroleum solution (b. p. 60—80°). This procedure (private communication from Dr. A. F. Millidge) is an improvement on that employing sodium ethoxide in alcohol.

Cyanohydrin (VIII).—A mixture of 25 g. of the keto-ester (VII) and 5 g. (30% excess) of hydrogen cyanide (Wade and Panting, J., 1898, **73**, 256) was cooled in ice, and a few drops of diethylamine added; a vigorous reaction took place. After standing overnight, the solid product was triturated with light petroleum (b. p. 40—60°) and collected. Crystallisation of the crude cyanohydrin (18·5 g.; 65%), m. p. 74°, from petroleum (b. p. 60—80°) afforded *ethyl 2-hydroxy-2-cyano-1 : 3-dimethyl*cyclo*hexane-1-carboxylate* (VIII) in massive aggregates of transparent

prisms, m. p. 75° (Found : C, 64·3 ; H, 8·6. $C_{12}H_{19}O_3N$ requires C, 64·0 ; H, 8·4%). The product was stable to keeping, but could not be distilled in a vacuum without serious decomposition.

Dehydration. The excess of hydrogen cyanide was removed in a vacuum from the crude cyanohydrin obtained from 50 g. of the keto-ester and 10 g. of hydrogen cyanide. The product was mixed with 40 g. (2 mols.) of pyridine and cooled in ice while 66 g. (2·2 mols.) of thionyl chloride were added dropwise with shaking during 25 minutes. The dark product was heated under reflux on the water-bath for an hour, poured on ice, and acidified. After filtration the liquid was extracted with ether, and the extract washed twice with 5% sodium hydroxide solution and with water. After drying, distillation afforded 34 g. of the unsaturated cyano-ester (IX), b. p. 116—120°/1·5 mm.; redistillation yielded 31 g. (60%) of a product, b. p. 112°/1 mm., which still contained some unchanged cyanohydrin (Found : C, 66·6; H, 8·4. Calc. for $C_{12}H_{17}O_2N$: C, 69·6; H, 8·2%. Calc. for $C_{12}H_{19}O_3N$: C, 64·0; H, 8·4%).

Acid hydrolysis. 10 G. of the unsaturated cyano-ester (IX) were refluxed for 5 days with 50 c.c. of concentrated hydrochloric acid. The product was poured into an excess of 10% sodium bicarbonate solution, ether extraction then affording some 4 g. of ketone derived from undehydrated cyanohydrin. The residual solution was acidified and thoroughly extracted with ether. Evaporation of the dried extract left 6·25 g. (60%) of an oil, which readily solidified in a vacuum desiccator. The product was drained on a porous tile and crystallised once from petroleum (b. p. 60—80°) and twice from benzene. 2-Carboxy-1 : 3-dimethyl-1 : 3-*cyclo*hexanolide (VI) (1·54 g.) so obtained formed feathery rosettes of prismatic needles, m. p. 145° (Found : C, 60·6; H, 7·2. Calc. for $C_{10}H_{14}O_4$: C, 60·6; H, 7·1%). Vocke (*loc. cit.*) gives m. p. 146°.

Alkaline hydrolysis. 12 G. of the unsaturated cyano-ester (IX) were refluxed for 5 days with 22 g. of potassium hydroxide in 175 c.c. of water. The product was cooled and extracted with ether to remove neutral by-products. The acidified solution was again extracted with ether; evaporation of the dried extract left 7·5 g. (70%) of a gum. This was refluxed for 3 hours with 10 g. of concentrated sulphuric acid in 200 c.c. of methyl alcohol. The greater part of the methyl alcohol was removed under reduced pressure, and the residue poured into water and extracted with ether. The extract was washed repeatedly with 10% sodium carbonate solution, dried, and evaporated; the residue, on standing, deposited 0·85 g. of a saturated nitrogenous solid, crystallisation of which from dilute methyl alcohol yielded *2-cyano-*1 : *3-dimethyl-*1 : 3-cyclo*hexanolide* in transparent plates, m. p. 168—169° (Found : C, 67·4, 67·1; H, 7·5, 7·5. $C_{10}H_{13}O_2N$ requires C, 67·0; H, 7·3%), which dissolved in warm dilute sodium hydroxide solution and were reprecipitated on acidification.

Acidification of the sodium carbonate washings, followed by extraction with ether and evaporation of the dried extract, yelded 1·7 g. of a product which rapidly solidified in a vacuum desiccator. After draining on a porous tile, two crystallisations from petroleum (b. p. 100—120°) yielded 0·5 g. of methyl hydrogen 1 : 3-dimethyl-Δ^2-*cyclo*hexane-1 : 2-dicarboxylate in rosettes of prismatic needles, m. p. 129—130° (Found : C, 62·3; H, 8·0. Calc. for $C_{11}H_{16}O_4$: C, 62·3; H, 7·6%). Vocke (*loc. cit.*) gives m. p. 132°.

Evaporation of the mother-liquors from the crystallisations yielded 0·75 g. of crude ester, which was refluxed for 4 hours with 1 g. of potassium hydroxide in 5 c.c. of ethyl alcohol. The alcohol was removed, and neutral material extracted with ether. The residual solution was acidified and again extracted with ether. Evaporation of the dried extract yielded a gum, which was thrice crystallised from acetic acid; in this way 0·11 g. of 1 : 3-dimethyl-Δ^2-*cyclo*hexene-1 : 2-dicarboxylic acid (V) was obtained in transparent prisms, m. p. 185° (decomp.) (Found : C, 60·9; H, 7·5. Calc. for $C_{10}H_{14}O_4$: C, 60·6; H, 7·1%). The same product was also obtained by direct hydrolysis of the crude monomethyl ester. A specimen of the unsaturated acid, $C_{10}H_{14}O_4$, prepared from abietic acid by Dr. Vocke had m. p. 181—183° (decomp.), and 183—185° (decomp.) when mixed with the synthetic acid.

Attempted Acid Hydrolysis of the Cyanohydrin (VIII).—The crude product from 25 g. of the keto-ester and 5 g. of hydrogen cyanide was refluxed for 72 hours with 150 c.c. of concentrated hydrochloric acid. Steam-distillation afforded a small amount of ketone together with a large amount of unchanged cyanohydrin, m. p. and mixed m. p. 73—75°. The residual solution deposited 3·5 g. of a neutral nitrogenous product, m. p. 255°, unchanged on crystallisation from dilute ethyl alcohol; this was not further investigated.

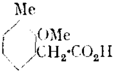
The author's thanks are due to Professor H. Wieland for supplying a specimen of the acid $C_{10}H_{14}O_4$, prepared by the late Dr. Vocke, and to the Government Grants Committee of the Royal Society for a grant.

IMPERIAL COLLEGE, LONDON, S.W. 7. [*Received, December 1st, 1936.*]

50. *Syntheses in the Phenanthrene Series. Part IV.* **1-*Methoxy-2-methylphenanthrene and the Preparation of Substituted Phenylacetic Acids.***

By Peter Hill and W. F. Short.

1-Methoxy-2-methylphenanthrene has been synthesised by Pschorr's method, *2-methoxy-*m*-tolylacetic acid* (I) being used as one component. 2-Methoxy-*m*-tolualdehyde (II), the starting point for the preparation of this acid, was obtained from *o*-cresotic acid (2-hydroxy-*m*-toluic acid) by methylation and reduction of the carboxyl group by one of the following series of reactions: (1) 2-methoxy-*m*-toluic acid ⟶ *2-methoxy-*m*-toluanilide* ⟶ *2-methoxy-*m*-toluanilideiminochloride* ⟶ *2-methoxy-*m*-tolylideneaniline* ⟶ 2-methoxy-*m*-tolualdehyde; (2) methyl 2-methoxy-*m*-toluate ⟶ *2-methoxy-*m*-toluhydrazide* ⟶ *2-methoxy-*m*-tolubenzenesulphonhydrazide* ⟶ 2-methoxy-*m*-tolualdehyde (compare McFadyen and Stevens, J., 1936, 584).



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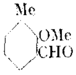

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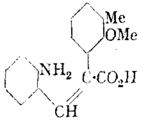

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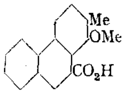
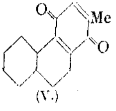


(IV.)

Condensation of the aldehyde with hippuric acid yielded *2-phenyl-4-(2′-methoxy-*m*-tolylidene)oxazolone*, which was successively hydrolysed to *2-methoxy-*m*-tolylpyruvic acid* and oxidised to 2-methoxy-*m*-tolylacetic acid. When the potassium salt of this acid was condensed with *o*-nitrobenzaldehyde, *2-nitro-α-(2′-methoxy-*m*-tolyl)cinnamic acid* was formed, together with some *o*-nitrocinnamic acid. The nitro-acid, which was obtained in two forms, yielded *2-amino-α-(2′-methoxy-*m*-tolyl)cinnamic acid* (III) on reduction with ferrous sulphate and ammonia. The corresponding diazonium salt was only slowly decomposed when shaken with copper powder, but when the solution was warmed with sodium carbonate *1-methoxy-2-methylphenanthrene-10-carboxylic acid* (IV) was rapidly formed. Decarboxylation was smoothly effected by heating with quinoline and copper powder. Oxidation of the resulting *1-methoxy-2-methylphenanthrene* produced an unexpected result. In place of the anticipated 9 : 10-quinone there was obtained a yellow compound, $C_{15}H_{10}O_2$, which we consider to be *2-methylphenanthrene-1 : 4-quinone* (V), since it did not yield a quinoxaline. Reductive acetylation furnished *1 : 4-diacetoxy-2-methylphenanthrene*.



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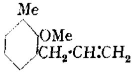

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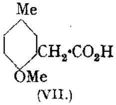


(VII.)

The preparation of substituted phenylacetic acids in quantity for use in the Pschorr synthesis is frequently attended with considerable difficulty and it occurred to us that they could be easily obtained from the corresponding allyl compounds, which are readily accessible. Reference to the literature showed, however, that oxidation of a large number of allyl compounds, even with ozone, invariably results in the production of a mixture of a phenylacetic acid and the corresponding benzoic acid. In order to explore the possibility of arresting the oxidation at the first stage, *3-allyl-o-tolyl methyl ether* (VI), obtained in excellent yield from *o*-tolyl allyl ether by rearrangement (Claisen and Eisleb, *Annalen*, 1913, **401**, 56) and methylation, was subjected to oxidation under a variety of conditions. When potassium permanganate was employed as oxidising agent, moderate yields of 2-methoxy-*m*-tolylacetic acid (I) were obtained if the reaction was conducted in

presence of alcohol (compare Higginbottom and Short, *Rec. trav. chim.*, 1934, **53**, 1141). The influence of the alcohol was traced to the production of acetic acid, and 40% yields of the tolylacetic acid were obtained when the requisite quantity of acetic acid was introduced at the outset, a considerable quantity of the allyl compound being recovered unchanged. Other methods of acidification gave less favourable results. The method appears to be general and we now describe the transformation of 3-bromo-*p*-tolyl methyl ether into *3-allyl-*p*-tolyl methyl ether* and *4-methoxy-*m*-tolylacetic acid* (VII).

Experimental.

*Methyl 2-Methoxy-*m*-toluate.*—A paste of *o*-cresotic acid (1 mol.) and 50% sodium hydroxide solution (2·4 mols.) was cautiously warmed with methyl sulphate (2·4 mols.). After the vigorous reaction, the product was washed with dilute sodium hydroxide solution to remove unchanged *o*-cresotic acid (8%), dried, and distilled. The resulting liquid, b. p. 116—125°/12 mm., which consisted of a mixture of methyl 2-methoxy-*m*-toluate with methyl 2-hydroxy-*m*-toluate (up to 30%), was remethylated with methyl sulphate (1·5 mols.) and sodium methoxide (from 1·5 atoms of sodium and 3 vols. of methyl alcohol) and afforded methyl 2-methoxy-*m*-toluate, b. p. 120°/12 mm., in an overall yield of 70%. Saponification now yielded pure 2-methoxy-*m*-toluic acid, m. p. 83—84°.

*2-Methoxy-*m*-toluanilide.*—The acid was warmed with thionyl chloride (3 mols.), the excess of the reagent removed under diminished pressure, and, after dilution with dry benzene, a dilute solution of aniline (2 mols.) in chloroform added at 0°. The *anilide*, b. p. *ca.* 210°/8 mm., separated from alcohol in long needles, m. p. 82·5—83° (Found: C, 74·6; H, 6·4; N, 5·9. $C_{15}H_{15}O_2N$ requires C, 74·7; H, 6·2; N, 5·8%). Yield, 65%.

*2-Methoxy-*m*-toluhydrazide*, obtained in almost quantitative yield from methyl 2-methoxy-*m*-toluate and 50% hydrazine hydrate (2·1 mols.) in alcohol, separated from benzene–light petroleum (b. p. 60—80°) in stout prisms, m. p. 79·5—80·5° (Found: C, 59·8; H, 6·8; N, 15·6. $C_9H_{12}O_2N_2$ requires C, 60·0; H, 6·7; N, 15·5%).

*2-Methoxy-*m*-tolubenzenesulphonhydrazide.*—The hydrazide was converted into the *benzenesulphonhydrazide* by the action of benzenesulphonyl chloride (1 mol.) and pyridine (10 mols.). The product, isolated in the usual way, crystallised from alcohol in rhombic prisms, m. p. 149—150° (Found: C, 56·4; H, 4·9. $C_{15}H_{16}O_4N_2S$ requires C, 56·3; H, 5·0%). The yield was 67%.

*2-Methoxy-*m*-tolualdehyde.*—(1) A solution of 2-methoxy-*m*-toluanilide in benzene (2 parts) was warmed at 50—110° for 1 hour with phosphorus pentachloride (1·1 mols.), the benzene and phosphorus oxychloride removed by distillation under diminished pressure, and the residue mixed with stannous chloride (3 mols.) dissolved in a saturated solution of hydrogen chloride in ether. After 3 days at room temperature, the yellow crystals were collected, acidified, and distilled with steam. The aldehyde, b. p. 118°/12 mm., was obtained in 62% yield and afforded a semicarbazone, m. p. 216—216·5°, which did not depress the m. p. of a specimen prepared by the Tiemann–Reimer method (Simonsen, J., 1918, **113**, 777). Substitution of thionyl chloride (3 mols.) for phosphorus pentachloride in the preparation of the iminochloride (compare v. Braun and Pinkernelle, *Ber.*, 1934, **67**, 1218) lowered the yield of aldehyde to 36%. (2) Anhydrous sodium carbonate (8·3 g.) was added to a solution of 2-methoxy-*m*-tolubenzenesulphonhydrazide (10 g.) in ethylene glycol (50 c.c.) at 160°, the temperature maintained at 150—160° for 4—5 minutes, hot water then added, and the aldehyde extracted with ether. The yield of aldehyde (b. p. 115—120°/12 mm.; semicarbazone, m. p. 216—216·5°) was 66%.

*2-Phenyl-4-(2′-methoxy-*m*-tolylidene)oxazolone.*—This *azlactone* was obtained in almost theoretical yield by heating a mixture of 2-methoxy-*m*-tolualdehyde, hippuric acid (1 mol.), sodium acetate (1 mol.), and acetic anhydride (3 mols.) on a boiling water-bath for 2 hours. It separated from benzene in fine yellow needles, m. p. 160—161° (Found: C, 73·65; H, 5·0; N, 4·9. $C_{18}H_{15}O_3N$ requires C, 73·7; H, 5·1; N, 4·8%).

*2-Methoxy-*m*-tolylpyruvic Acid.*—When the azlactone was boiled for 5 hours with 10% sodium hydroxide solution (5 parts), and the product freed from benzoic acid by the sulphur dioxide method, the *pyruvic acid* was obtained in satisfactory yield. It separated from chloroform in colourless plates, m. p. 131—132° (Found: C, 63·7; H, 5·9. $C_{11}H_{12}O_4$ requires C, 63·5; H, 5·8%).

*2-Methoxy-*m*-tolylacetic Acid.*—An ice-cold solution of sodium 2-methoxy-*m*-tolylpyruvate in 10% aqueous sodium hydroxide was oxidised by a slight excess of 6% hydrogen peroxide. Next day the *tolylacetic acid* was precipitated by dilute sulphuric acid, dried, and recrystallised

from light petroleum (b. p. 60—80°); it formed large rectangular plates, m. p. 98·6—99·6° (Found: C, 66·8; H, 6·6. $C_{10}H_{12}O_3$ requires C, 66·7; H, 6·7%).

2-*Nitro-α-(2′-methoxy-*m*-tolyl)cinnamic Acid*.—A mixture of potassium 2-methoxy-*m*-tolylacetate (dried at 130°), *o*-nitrobenzaldehyde (1·2 mols.), and acetic anhydride (10 mols.) was heated under reflux at 100° for 26 hours. Water was then added to destroy the acetic anhydride, and the residual pasty mass was taken up in ether and repeatedly extracted with sodium hydroxide solution to separate a considerable quantity of the nitrostilbene. The solid precipitated by acidifying the alkaline solution consisted of a mixture of 2-*nitro-α-(2′-methoxy-*m*-tolyl)cinnamic acid* and 2-nitrocinnamic acid, which was separated by extraction with benzene, in which the second acid is relatively insoluble. 2-Nitro-α-(2′-methoxy-*m*-tolyl)cinnamic acid, obtained in 40—66% yield, crystallised from chloroform–light petroleum in rhombs elongated along one axis, m. p. 180—181° (Found: C, 65·1: H, 5·0; N, 4·6. $C_{17}H_{15}O_5N$ requires C, 65·2; H, 4·8; N, 4·4%). In one instance, the acid was obtained in stout hexagonal prisms, m. p. 198—199° (Found: C, 65·3; H, 4·8%). Both forms afforded the same amino-acid on reduction.

2-*Amino-α-(2′-methoxy-*m*-tolyl)cinnamic Acid*.—A hot ammoniacal solution of the nitro-acid was added to a reducing mixture prepared from crystalline ferrous sulphate (7·7 mols.) and excess of ammonia. After heating at 100° for 2 hours, the solution was filtered, and the *amino-acid* precipitated by dilute hydrochloric acid (yield, *ca.* 60%). This acid crystallised from absolute alcohol in long clustered rods, m. p. 188—188·5° (Found: N, 4·9. $C_{17}H_{17}O_3N$ requires N, 4·9%).

1-*Methoxy-2-methylphenanthrene-10-carboxylic Acid*.—A solution of the amino-acid in an equivalent of dilute aqueous sodium hydroxide was added to 2*N*-sulphuric acid (10 mols.) at 0° and the calculated quantity of *M*-sodium nitrite was then added slowly. As diazotisation was slow, the mixture was kept at 0° for 12 hours, and the small residue removed by filtration. The clear diazonium solution was only slowly decomposed on shaking with copper powder, but decomposition was complete in 10 minutes when the red solution, obtained by making alkaline with sodium carbonate, was heated on the water-bath. The solution was acidified with dilute sulphuric acid at 0°, and the *acid* recrystallised from acetic acid. It was obtained in almost colourless, stout prisms, m. p. 186·3—187·3° (Found: C, 77·0; H, 5·3. $C_{17}H_{14}O_3$ requires C, 76·7; H, 5·2%).

1-*Methoxy-2-methylphenanthrene*.—The acid was smoothly decarboxylated by heating at 230° for 2¾ hours with 1/10th of its weight of copper powder and 5 parts of quinoline. The neutral *product* crystallised from methyl alcohol in colourless flakes, m. p. 82·5—83° (Found: C, 86·1; H, 6·6. $C_{16}H_{14}O$ requires C, 86·5; H, 6·3%). The *picrate* separated from alcohol in orange-yellow needles, m. p. 127·5—128° (Found: C, 58·7; H, 3·7; N, 9·4. $C_{16}H_{14}O,C_6H_3O_7N_3$ requires C, 58·6; H, 3·8; N, 9·3%). When 1-methoxy-2-methylphenanthrene (0·6 g.), dissolved in acetic acid (3 c.c.), was oxidised below 70° with a solution of chromic anhydride (1·2 g.) in water (0·8 c.c.) and acetic acid (7·2 c.c.), a light yellow solid was deposited on cooling. Recrystallisation from alcohol afforded long orange-yellow needles, m. p. 153—154° (Found: C, 81·0; H, 4·7; *M*, Rast, 236. $C_{15}H_{10}O_2$ requires C, 81·1; H, 4·5%; *M*, 222). When this 2-*methylphenanthrene*-1 : 4-*quinone* was warmed with zinc dust, acetic anhydride and pyridine, it was reduced to 1 : 4-*diacetoxy-2-methylphenanthrene*, which separated from benzene–light petroleum in long colourless rods, m. p. 165—165·5° (Found: C, 74·2; H, 5·15. $C_{19}H_{16}O_4$ requires C, 74·0; H, 5·2%).

3-*Allyl-o-tolyl Methyl Ether*.—In the conversion of *o*-cresol into *o*-tolyl allyl ether and 3-allyl-*o*-cresol (Claisen and Eisleb, *loc. cit.*), 90% and 81% yields were obtained. The phenol was methylated without isomerisation of the side chain when 10% sodium hydroxide solution (2·25 mols.) and methyl sulphate (2·0 mols.) were added alternately below 60°. The *methyl ether* (yield, 81%) was obtained as a colourless liquid, b. p. 94—96°/10 mm. (Found: C, 81·6; H, 8·5. $C_{11}H_{14}O$ requires C, 81·5; H, 8·6%).

Oxidation of 3-Allyl-o-tolyl Methyl Ether.—After numerous trials with hydrogen peroxide and potassium permanganate, the following process was devised for the preparation of the phenylacetic acid. A mixture of the methyl ether with ice-water (100 vols.) and acetic acid (7·2 mols.) was cooled in a freezing mixture and stirred into an emulsion. Potassium permanganate (5%: equivalent to 6 atoms of oxygen) was then added at such a rate that the temperature remained below 1°. Unchanged methyl ether (13—20%) was removed in steam, the mixture made alkaline with dilute sodium hydroxide solution, filtered, and evaporated to a small volume. Acidification of the red liquid to litmus with hydrochloric acid afforded a sticky red precipitate, which was removed by decantation, and further addition of acid (Congo-red)

then precipitated the bulk of the 2-*methoxy*-m-*tolylacetic acid* in almost pure condition. The aqueous layer was extracted with ether, and the red precipitate (above) dissolved in the solution, which was then dried and evaporated. Distillation of the residue under diminished pressure afforded (1) acetic acid; (2) almost pure 2-methoxy-*m*-tolylacetic acid, b. p. 187—189°/10 mm., and (3) a small quantity of a red semi-solid mass containing some tolylacetic acid. Only traces of 2-methoxy-*m*-toluic acid were present, so the crude acid was easily purified by crystallisation from light petroleum. The average yield of 2-methoxy-*m*-tolylacetic acid, calculated on the 3-allyl-*o*-tolyl methyl ether employed, was 40% of the theoretical.

4-Methoxy-m-*tolylacetic Acid*.—Dropwise addition of allyl bromide (1·1 mols.) to the Grignard compound of 3-bromo-*p*-tolyl methyl ether (J., 1936, 323), followed by boiling for 3 hours, afforded 3-allyl-*p*-tolyl methyl ether, b. p. 100—125°/10 mm., in 50% yield.* Oxidation of this ether under the conditions specified above for 3-allyl-*o*-tolyl methyl ether furnished 4-*methoxy*-m-*tolylacetic acid*, m. p. 131—132° (Found: C, 66·9; H, 6·6. $C_{10}H_{12}O_3$ requires C, 66·7; H, 6·7%).

We are indebted to the Chemical Society for a grant.

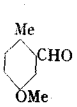
THE COLLEGE OF TECHNOLOGY, MANCHESTER. [*Received, November 20th*, 1936.]

51. *Syntheses in the Phenanthrene Series. Part V. 4-Methoxy-1-methylphenanthrene.*

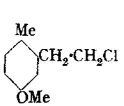
By ALICE HIGGINBOTTOM, PETER HILL, and W. F. SHORT.

IN attempting the synthesis of 4-*methoxy*-1-*methylphenanthrene* (IV) we first prepared 4-*methoxy*-o-*tolualdehyde* (I). For this purpose *p*-nitrotoluene was converted successively into 2-bromo-4-nitrotoluene, 2-bromo-*p*-toluidine and 2-bromo-*p*-cresol. This phenol was isolated in an unstable form, m. p. 16°, which subsequently changed into the stable form, m. p. 55°, described in the patent literature (D.R-P. 15,633). Methylation gave 2-bromo-*p*-tolyl methyl ether, the Grignard compound of which was converted into the required aldehyde on heating with ethyl orthoformate. Alternatively, the Grignard compound was carbonated and the chloride of the resulting 4-*methoxy*-o-*toluic acid* reduced to the aldehyde by Rosenmund's method. No condensation product could, however, be obtained from 4-methoxy-*o*-tolualdehyde and sodium *o*-nitrophenylacetate; the aldehyde was recovered and the sodium salt converted into *o*-nitrotoluene.

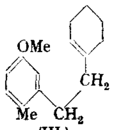
In the next attempt, β-(4-*methoxy*-o-*tolyl*)*ethyl chloride* (II) was prepared from the Grignard compound of 2-bromo-*p*-tolyl methyl ether and β-chloroethyl toluene-*p*-sulphonate (compare Ferns and Lapworth, J., 1912, **108**, 273; Gilman and Beaber, *J. Amer. Chem. Soc.*, 1923, **45**, 839). The Grignard compound of this chloride and *cyclo*hexanone afforded 1-β-(4′-*methoxy*-o-*tolyl*)*ethyl*cyclo*hexan*-1-*ol*, accompanied by a small amount of αδ-*di*-(4-*methoxy*-o-*tolyl*)*butane*. The yield of carbinol was low and we have observed that a methoxy-group, especially when present in the *o*-position, depresses the yield both of the carbinol and of the tricyclic compound produced from it at a later stage. The alcohol was



(I.)



(II.)



(III.)

(IV.)

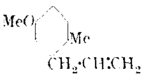
dehydrated to 1-β-(4′-*methoxy*-o-*tolyl*)*ethyl*-Δ¹-cyclo*hexene* (III), which, on treatment with aluminium chloride, afforded a mixture of substances from which we were unable to isolate a homogeneous fraction by distillation. On the assumption that the mixture contained 5-methoxy-8-methyl-1 : 2 : 3 : 4 : 9 : 10 : 11 : 12-octahydrophenanthrene, it was dehydrogenated with sulphur. A sparingly soluble *picrate*, m. p. 182—183°, was isolated from the

* We are grateful to Miss A. Higginbottom for this preparation.

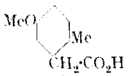
distillate, and ammonia liberated a *compound*, m. p. 78·5—79°, giving the correct analytical figures for 4-methoxy-1-methylphenanthrene (IV).

Cook and his collaborators (J., 1933, 1101; 1934, 365) have shown that there is a tendency for compounds of type (III) to yield spirans in addition to or instead of phenanthrenes. In this instance the formation of a spiran appeared to be excluded by the analytical figures, but the synthesis could not be regarded as satisfactory since insufficient material was available for a detailed examination of the product. It was therefore decided to apply the simple and convenient method for the preparation of substituted phenylacetic acids described in Part IV (preceding paper) to the synthesis of 4-methoxy-1-methylphenanthrene by an unambiguous method.

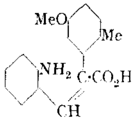
The Grignard compound of 2-bromo-*p*-tolyl methyl ether (above) and allyl bromide furnished *2-allyl-p-tolyl methyl ether* (V), which was oxidised to *4-methoxy-o-tolylacetic acid* (VI).



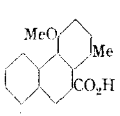
(V.)



(VI.)



(VII.)



(VIII.)

The sodium salt of this acid and *o*-nitrobenzaldehyde yielded *2-nitro-α-(4'-methoxy-o-tolyl)-cinnamic acid*, which was reduced to the corresponding *amino-acid* (VII). When a solution of the diazonium salt of (VII) was heated, *4-methoxy-1-methylphenanthrene-10-carboxylic acid* (VIII) was obtained and decarboxylation furnished 4-methoxy-1-methylphenanthrene identical with that obtained by the first method. Demethylation of (IV) gave *4-hydroxy-1-methylphenanthrene*.

EXPERIMENTAL.

2-Bromo-4-nitrotoluene.—Scheufelen (*Annalen*, 1885, **231**, 171) brominated *p*-nitrotoluene in presence of ferrous bromide in a sealed tube at 70°; by substituting iron powder as catalyst, a 70% yield of 2-bromo-4-nitrotoluene was obtained in open vessels. Bromine (100 c.c.) was added during 3 hours to *p*-nitrotoluene (280 g.) and iron powder (10 g.) at 95—100°. The mixture was heated for ¾ hour and the oil, obtained by pouring into hot water, was washed with sodium bisulphite solution and hydrochloric acid. The oil, which solidified on cooling, melted at 76—77° after washing with water, and was sufficiently pure for reduction.

2-Bromo-p-toluidine.—Scheufelen (*loc. cit.*) reduced 2-bromo-4-nitrotoluene with tin and hydrochloric acid, but does not record the yield obtained. A 95% yield of 2-bromo-*p*-toluidine was obtained from 2-bromo-4-nitrotoluene (43 g.), concentrated hydrochloric acid (2 c.c.), alcohol (100 c.c.), and reduced iron powder (34 g.); West's technique (J., 1925, **127**, 494) was used, but the mixture was boiled for 9 hours after addition of the iron. The amine melted at 26—27° and afforded a *benzoyl* derivative, m. p. 132° (Found: N, 4·9. $C_{14}H_{12}ONBr$ requires N, 4·8%).

2-Bromo-p-cresol.—The conversion of 2-bromo-*p*-toluidine into 2-bromo-*p*-cresol, m. p. 55—56°, is recorded by the Badische Anilin- & Soda-Fabrik (Friedländer's "Fortschritte," 1905, **8**, 203), but no details are given. A 68% yield of the phenol was obtained when the diazonium solution, prepared from the base (10 g.), concentrated hydrochloric acid (6 c.c.), water (40 c.c.), and sodium nitrite (3·5 g.) at 0°, was slowly added to anhydrous sodium sulphate (420 g.), concentrated sulphuric acid (200 c.c.), and water (150 c.c.) at 120—130°. The phenol was removed in a current of superheated steam as it was formed. The first preparation melted sharply at 16°, but was transformed into the stable form, m. p. 54·5—55°, when inoculated with a crystal obtained in a subsequent experiment. Both forms afforded the same *benzoate*, m. p. 74·5—75·5° (Found: C, 57·7; H, 3·9; Br, 27·5. $C_{14}H_{11}O_2Br$ requires C, 57·7; H, 3·8; Br, 27·5%). Methylation with methyl sulphate (1·4 mols.) and 10% sodium hydroxide solution afforded 2-bromo-*p*-tolyl methyl ether, b. p. 103—105°/10 mm., in 72% yield and 8% of phenol was recovered.

4-Methoxy-o-toluic Acid.—Excess of solid carbon dioxide was added to a Grignard solution from the preceding bromo-ether (20 g.), magnesium (2·4 g.), and ether (50 c.c.) and, after standing for an hour, the complex was decomposed in the usual way. The *acid* (yield 31%) was recrys-

tallised from hot water and melted at 142° (Found : C, 65·0; H, 6·2. $C_9H_{10}O_3$ requires C, 65·1; H, 6·0%). The chloride, b. p. 125—126°/10 mm., was obtained in 86% yield from the acid and excess of thionyl chloride.

4-*Methoxy*-o-*tolualdehyde*.—(1) Ethyl orthoformate (7·4 g.) was added to a Grignard solution prepared from 2-bromo-*p*-tolyl methyl ether (20 g.), magnesium (2·4 g.), and ether (50 c.c.), and the complex decomposed with ice-cold hydrochloric acid. The oil, obtained from the ethereal layer, was boiled with 5*N*-hydrochloric acid to hydrolyse the acetal, and the aldehyde, b. p. 120°/11 mm., isolated in the usual way (yield 34%). It afforded a *semicarbazone*, m. p. 212—213° (Found : C, 58·2; H, 6·3; N, 20·1. $C_{10}H_{13}O_2N_3$ requires C, 58·0; H, 6·3; N, 20·3%). (2) A poor yield (13%) of the aldehyde (semicarbazone, m. p. 212—213°) was obtained by reducing 4-methoxy-*o*-toluoyl chloride (6 g.), dissolved in xylene (50 c.c.), in presence of palladium–barium sulphate (4 g.) (Schmidt, *Ber.*, 1919, **52**, 409).

β-(4-*Methoxy*-o-*tolyl*)*ethyl Chloride*.—β-Chloroethyl toluene-*p*-sulphonate (47 g.) in benzene (100 c.c.) was added to a solution of the Grignard compound of 2-bromo-*p*-tolyl methyl ether (from 4·8 g. of metal and 30·2 g. of the bromo-ether in 45 c.c. of ether), and the mixture warmed to 55°. A white solid separated and the temperature was maintained for an hour by the heat of the reaction. After 12 hours, the mixture was refluxed for 1 hour and then hydrolysed in the usual manner. Careful fractionation gave a 43% yield of β-(4-*methoxy*-o-*tolyl*)*ethyl chloride*, b. p. 126—134°/10 mm. A middle fraction, b. p. 132—133°/10 mm., was analysed (Found : Cl, 19·0. $C_{10}H_{13}OCl$ requires Cl, 19·2%).

1-β-(4′-*Methoxy*-o-*tolyl*)*ethyl*cyclo*hexan*-1-*ol*.—A cold solution of *cyclo*hexanone (48 c.c.) in ether (100 c.c.) was slowly added with stirring to the Grignard compound of the preceding chloride (48 g.; metal 18·8 g.; ether 400 c.c.) cooled in a freezing mixture. After 12 hours, the mixture was decomposed with acidified ammonium chloride solution, and the ethereal layer washed, dried, and evaporated. Repeated fractionation of the residue afforded (1) 1-β-(4′-*methoxy*-o-*tolyl*)*ethyl*cyclo*hexan*-1-*ol* as a viscous oil, b. p. 175—180°/4 mm. (Found: C, 77·8; H, 9·4. $C_{16}H_{24}O_2$ requires C, 77·4; H, 9·7%) (yield, 40%), and (2) a smaller fraction, b. p. 200—220°/5 mm., which solidified on cooling. Recrystallisation from methyl alcohol gave 3·2 g. of αδ-*di*-(4-*methoxy*-o-*tolyl*)*butane*, m. p. 105—106° (Found : C, 80·5; H, 8·5. $C_{20}H_{26}O_2$ requires C, 80·5; H, 8·7%).

1-β-(4′-*Methoxy*-o-*tolyl*)*ethyl*-Δ¹-cyclo*hexene* (III).—Dehydration of the carbinol by heating for 1¼ hours at 160—170° with potassium hydrogen sulphate (1·5 parts) gave a 94% yield of the cyclo*hexene* derivative as a pale yellow liquid, b. p. 150—155°/4 mm. (Found : C, 83·2; H, 9·25. $C_{16}H_{22}O$ requires C, 83·5; H, 9·6%).

2-*Allyl*-p-*tolyl Methyl Ether*.—Allyl bromide (1·1 mols.) was added to a Grignard solution prepared from 2-bromo-*p*-tolyl methyl ether (1 mol.), magnesium (1 atom), and ether (5 mols.) so that the mixture boiled gently. After standing for 12 hours, the solution was boiled for 3 hours, and the product decomposed with ice-cold dilute sulphuric acid, washed, and fractionated. The portion, b. p. 100—105°/10 mm., was a pleasant-smelling liquid (yield, 60%) and a fraction, b. p. 102—104°/10 mm., was analysed (Found : C, 82·0; H, 8·7. $C_{11}H_{14}O$ requires C, 81·5; H, 8·6%).

4-*Methoxy*-o-*tolylacetic Acid*.—The aforesaid unsaturated compound was oxidised with 5% potassium permanganate solution and acetic acid exactly as in the preparation of the isomeric 4-methoxy-*m*-tolylacetic acid (preceding paper). The yield (21%) was considerably lower, but 33% of the unsaturated compound was recovered. 4-*Methoxy*-o-*tolylacetic acid* separated from light petroleum (b. p. 60—80°) in large rectangular plates, m. p. 103—104° (Found : C, 66·7; H, 6·7. $C_{10}H_{12}O_3$ requires C, 66·7; H, 6·7%).

2-*Nitro*-α-(4′-*methoxy*-o-*tolyl*)*cinnamic Acid*.—Potassium 4-methoxy-*o*-tolylacetate (1 mol., dried at 130°), *o*-nitrobenzaldehyde (1 mol.), and acetic anhydride (10 mols.) were maintained at 100° for 27 hours; water was then added, and the product isolated in the normal manner. The condensation *product* crystallised from benzene in almost colourless plates, m. p. 177—178° (Found : C, 65·1; H, 4·8; N, 4·55. $C_{17}H_{15}O_5N$ requires C, 65·2; H, 4·8; N, 4·4%). The yield was 51% and a small amount of *o*-nitrocinnamic acid was obtained as a by-product.

2-*Amino*-α-(4′-*methoxy*-o-*tolyl*)*cinnamic Acid*.—The nitro-compound was reduced at 100° with ferrous sulphate (7·7 mols.) and aqueous ammonia; the *amino-acid* (yield 79%) crystallised from alcohol in rhombic plates, m. p. 178—179° (Found : C, 72·1; H, 6·2; N, 4·9. $C_{17}H_{17}O_3N$ requires C, 72·1; H, 6·0; N, 4·9%).

4-*Methoxy*-1-*methylphenanthrene*-10-*carboxylic Acid*.—The above amino-acid (7·7 g.) was converted into the sulphate by adding 2*N*-sulphuric acid (98 c.c.) and methyl alcohol (123 c.c.), and the fine suspension diazotised at 0° by adding *M*-sodium nitrite (27 c.c.). Stirring was continued for 12 hours and the solution filtered (4·8 g. of amino-acid, crystallised once from benzene, m. p. 178—179°, were recovered). The filtrate was boiled, the precipitate collected, and the

acid separated by extraction with sodium carbonate solution. It crystallised from acetic acid *in small sandy rhombs, m. p. 213·5—214° (Found: C, 76·8; H, 5·3. $C_{17}H_{14}O_3$ requires C, 76·7; H, 5·2%).*

4-Methoxy-1-methylphenanthrene.—(1) Powdered aluminium chloride (34 g.) was added to an ice-cold solution of 1-β-(4′-methoxy-*o*-tolyl)ethyl-Δ¹-*cyclo*hexene (22·5 g.) in carbon disulphide (380 g.). After being kept at 0° for 24 hours, the mixture was decomposed with hydrochloric acid and ice. Since no homogeneous fraction could be isolated from the product by distillation, the whole (20·7 g., b. p. 130—162°/5 mm.) was mixed with sulphur (6·7 g.) and heated to 235° during 5 hours. The mixture was then distilled under diminished pressure, and the distillate boiled with excess of alcoholic picric acid. The resulting *picrate* (1·0 g.) separated from alcohol in tawny orange needles, m. p. 182—183° (Found: C, 58·8; H, 4·0; N, 9·3. $C_{16}H_{14}O,C_6H_3O_7N_3$ requires C, 58·5; H, 3·8; N, 9·3%). *4-Methoxy-1-methylphenanthrene*, regenerated from the pure picrate, separated from methyl alcohol in long rods, m. p. 78·5—79° (Found: C, 86·7; H, 6·4. $C_{16}H_{14}O$ requires C, 86·5; H, 6·3%). (2) Decarboxylation of 4-methoxy-1-methylphenanthrene-10-carboxylic acid (0·3 g.) was effected by heating with copper powder (0·15 g.) and quinoline (1·5 c.c.) for 2 hours at 230°. The product, purified by crystallisation from methyl alcohol, melted at 78·5—79° and afforded a picrate, m. p. 182—183°. There were no depressions of m. p.'s when the two substances last described were mixed with the corresponding compounds prepared by method (1).

4-Hydroxy-1-methylphenanthrene.—The methoxy-compound (0·2 g.), acetic acid (4 c.c.), and hydriodic acid (4 c.c., *d* 1·7) were boiled for 4½ hours, and the phenol (0·16 g.) isolated in the usual way. *4-Hydroxy-1-methylphenanthrene* crystallised from chloroform–ligroin in colourless needles, m. p. 103—104° (Found: C, 86·4; H, 5·9. $C_{15}H_{12}O$ requires C, 86·5; H, 5·8%), and gave an olive-green coloration with aqueous ferric chloride. The *benzoate* separated from chloroform–methyl alcohol in prisms, m. p. 121—122° (Found: C, 84·2; H, 5·3. $C_{22}H_{16}O_2$ requires C, 84·6; H, 5·1%).

The authors are indebted to Imperial Chemical Industries, Limited, for gifts of chemicals and to the Chemical Society for a grant.

The College of Technology, Manchester. [*Received, November 28th, 1936.*]

52. *Orientation Effects in the Diphenyl Series. Part XIII. The Nitration of the Four 2-Halogeno-4 : 4′-dimethyldiphenyls.*

By Elizabeth E. J. Marler and E. E. Turner.

The observation (Shaw and Turner, J., 1932, 285; Marler and Turner, *ibid.*, p. 2391) that nitration of 4 : 4′-dihalogeno- and 4 : 4′-dimethyl-diphenyls tends to occur in the 2-position made it desirable to examine the more complicated cases of the nitration of the four 2-halogeno-4 : 4′-dimethyldiphenyls. The preparation of these compounds entailed an exceptional amount of tedious work, owing partly to the initial difficulty of making reasonable quantities of 4 : 4′-ditolyl and partly to the occurrence of unwanted side reactions during the replacement of a 2-amino-group (from 2-nitro-) by halogen. *2-Fluoro-* and *2-chloro-4 : 4′-dimethyldiphenyl* melt respectively at 73—74° and 32—33°, but the *2-bromo-* and *2-iodo-*compounds are liquids. It may be noted that 2-chlorodiphenyl is a solid, but that the corresponding bromo- and iodo-compounds are liquids. It is possible that with increase in size of the halogen atom from fluorine to iodine the diphenyl molecule is less able to take up a co-planar arrangement, and this would inevitably react on the shape of the crystal and on the melting point.

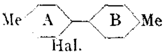
Mononitration of 2-fluoro-4 : 4′-ditolyl was accomplished without difficulty by the use of excess of equal volumes of nitric acid (*d* 1·2) and glacial acetic acid. Only one substance was formed, and this must be *2-fluoro-2′-nitro-4 : 4′-dimethyldiphenyl*, since reduction, followed by replacement of the amino-group by fluorine, gave *2 : 2′-difluoro-4 : 4′-dimethyldiphenyl*, identical with the substance obtained by a similar replacement from 2 : 2′-diamino-4 : 4′-dimethyldiphenyl.

In the nitration of the other three 2-halogeno-4 : 4′-ditolyls, difficulty was experienced in finding conditions which avoided both partial absence of nitration and partial dinitration.

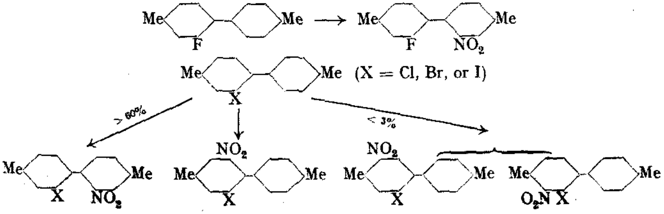
By using 1·5—2 molecular proportions of nitric acid (*d* 1·5) in an equal volume of glacial acetic acid in the warm, the second, more undesirable, difficulty was overcome. In all three cases, mixtures of nitro-compounds were obtained, and these could not be separated as such. Reduction, followed by conversion into mixtures of base hydrochlorides, rendered a partially quantitative separation possible, for one series of bases (α) formed sparingly soluble hydrochlorides, and were thus separable from the accompanying bases (β), which were most conveniently manipulated as their acetyl derivatives. By repeating the nitrations many times, we were able to satisfy ourselves that the figures for the weight proportion β/α for the chloro-, bromo- and iodo-compounds were, respectively, 2·7, 1·7 and 2·4.

The β-chloro- and β-iodo-bases were respectively convertible into 2 : 2′-dichloro- and 2 : 2′-di-iodo-4 : 4′-dimethyldiphenyl, though difficulties were encountered in performing the necessary replacements such as were noted, in similar work, by Mascarelli and his co-workers (*Gazzetta*, 1929, **59**, 858; 1931, **61**, 320) and by Angelletti and Brambilla (*ibid.*, 1930, **60**, 967). 2-Chloro- and 2-iodo-ditolyl are therefore nitrated to the extent of over 60% in position 2′. The constitution of the corresponding bromo-compound could not be proved and is inferred, and here again over 60% of 2′-nitration took place.

In view of the known deactivating effects of the halogens, particularly of fluorine, it would be expected that 2-fluoroditolyl would be mononitrated mainly or entirely in nucleus B. It has already been shown (*loc. cit.*) by the exclusive 2-nitration of 4 : 4′-ditolyl that the directive influence of the *p*-tolyl radical can entirely outweigh that of the methyl group. Apparently the *p*-tolyl radical can still exert its influence even when it contains a fluorine atom in position 2. This persistence of *ortho*-directive power by an aromatic nucleus with fluorine as a substituent has already been shown by the exclusive 2-nitration of 4 : 4′-difluorodiphenyl. For similar reasons, it would be expected that 2-chloro- and 2-bromo-ditolyl should be mononitrated mainly in nucleus B, in the 2′-position, but to a less extent than 2-fluoroditolyl, the electron affinities of these halogens being smaller. 2-Iododitolyl might be expected to undergo partial nitration in nucleus A, since iodine is feebly activating. The experimental fact is, however, that 2-iododitolyl actually gives more 2′-nitro-compound than does 2-bromoditolyl. One explanation of this is that the iodine atom, on account of its size, is near enough to the 2′-positions in nucleus B to have a Bennett " reversed-field " effect upon it.



The structure of the α-bases has not been settled, nor do we think that the elaborate investigation necessary to do this would lead to results of sufficient importance to justify it. That the α-bases are derived from neither a 3- nor a 5-nitro-compound is shown fairly conclusively by the observation that the total mononitration product in no instance responded to a sufficient extent to the hot piperidine test for activated halogen, the deactivating effect of methyl groups notwithstanding. We think that substitution in the 6-position is more likely than in the 3′-position, from a general consideration of the orienting effect of the tolyl group compared with that of the methyl group, in conjunction with the relative deactivating effects of the halogens. The whole of the results now obtained may be summarised in the scheme given below. The observed slight reactivity of the mononitro-mixtures with piperidine, which could be determined with considerable accuracy, fixes the amount of 3- or 5-nitration at not more than 3% :



EXPERIMENTAL.

2-Amino-4 : 4'-dimethyldiphenyl.—Reduction of 2-nitro-4 : 4'-ditolyl with iron filings and feebly acidified water at 100° was found more convenient than the method previously described (Marler and Turner, *loc. cit.*). The reduction mixture was extracted with boiling acetone, and the latter filtered and evaporated. The residual base was dissolved in hot dilute hydrochloric acid and the solution filtered from a little tarry dimethylcarbazole. The sparingly soluble hydrochloride was obtained on cooling, in 80% yield.

2-Fluoro-4 : 4'-dimethyldiphenyl.—20 G. of the preceding base were diazotised in hydrochloric acid and hydrofluoboric acid was added to the resulting solution until precipitation was complete. The precipitate was collected, washed with ether, and dried in a vacuum. The diazonium borofluoride (21 g.) was introduced in small quantities into a large flask heated at 100°. When decomposition was complete, the residue was treated with alkali and distilled in steam. *2-Fluoro-4 : 4'-dimethyldiphenyl* (11 g.) came over and was crystallised from methyl alcohol. It formed needles, m. p. 73—74° (Found : C, 83·3; H, 6·4. $C_{14}H_{13}F$ requires C, 83·9; H, 6·5%).

Nitration of 2-Fluoro-4 : 4'-dimethyldiphenyl.—6 G. of the fluoro-compound were dissolved in 30 c.c. of glacial acetic acid and 30 c.c. of nitric acid (*d* 1·43) were added. The fluorodimethyldiphenyl was precipitated in the cold, but after 2 minutes at 100° it all redissolved. The solution was poured into excess of water, a yellow oil separating which solidified later (7·2 g.). Crystallisation from alcohol gave 6·3 g. of small, pale yellow prisms, m. p. 89—90°. The theoretical yield of *2-fluoro-2'-nitro-4 : 4'-dimethyldiphenyl* is 7·6 g. (Found : N, 5·9. $C_{14}H_{12}O_2NF$ requires N, 5·7%).

Reduction of 2-Fluoro-2'-nitro-4 : 4'-dimethyldiphenyl.—The nitro-compound was reduced with stannous chloride in a mixture of acetic and hydrochloric acids at 100°. The cooled solution was poured into excess of alkali, and the base extracted with ether. The ether was evaporated and the residue dissolved in hot dilute hydrochloric acid. The hydrochloride separated in leaflets from the cooled solution, and from it was obtained *2-fluoro-2'-amino-4 : 4'-dimethyldiphenyl* which crystallised from aqueous alcohol in rectangular needles, m. p. 105—106° (yield, 96%) (Found : N, 6·5. $C_{14}H_{14}NF$ requires N, 6·5%).

2 : 2'-Difluoro-4 : 4'-dimethyldiphenyl.—6 G. of 2-fluoro-2'-aminoditolyl were dissolved in 20 c.c. of hydrofluoboric acid and 2 g. of sodium nitrite were added with stirring, the solution being well cooled. The diazonium borofluoride (8 g.) separated and was collected, washed with ether, and dried. It was decomposed at 100° and the product was distilled in steam; the difluoro-compound came over and readily solidified. It crystallised from alcohol in long needles (4 g.), m. p. 97—98°, and was identical with *2 : 2'-difluoro-4 : 4'-dimethyldiphenyl* obtained by decomposition of the bisdiazonium borofluoride prepared by a similar method from 2 : 2'-diamino-4 : 4'-ditolyl (Found : C, 76·9; H, 5·8. $C_{14}H_{12}F_2$ requires C, 77·0; H, 5·5%).

2-Chloro-4 : 4'-dimethyldiphenyl.—46 G. of the 2-amino-compound were submitted to a Sandmeyer reaction, and the product distilled in steam. Ditolyl (4 g.) came over first and then 24 g. of *2-chloro-4 : 4'-dimethyldiphenyl*. Crystallisation from methyl alcohol gave 20 g. of long needles, m. p. 32—33° (Found : Cl, 16·0. $C_{14}H_{13}Cl$ requires Cl, 16·4%).

Nitration of 2-Chloro-4 : 4'-dimethyldiphenyl.—5 G. of chloroditolyl were melted and 2 c.c. (1·8 mols.) of nitric acid (*d* 1·5) in 2 c.c. of glacial acetic acid were added slowly. The mixture became hot, but the oil did not all dissolve. It was heated for 5 minutes at 100°; the oil then dissolved, but reappeared on cooling. The mixture was poured into water, the oil extracted with ether, and the ether removed. It was impossible to cause the product to solidify (yield, 95%).

Reduction of Preceding Nitration Product.—This was effected with stannous chloride in acetic-hydrochloric acid at the b. p. The solution was strongly basified with alkali and extracted with ether, the latter then being removed. The residue was extracted several times with hot dilute hydrochloric acid, which left undissolved a little black oil. The filtered extracts on cooling deposited brownish crystals of a base hydrochloride (α), which was hydrolysed by water and was sparingly soluble in dilute hydrochloric acid. The mother-liquor was concentrated to half volume. On cooling, a brown gum and later small crystals appeared, the whole being treated as base hydrochloride (β). Addition of ammonia, followed by ether extraction, etc., gave a residue which was dissolved in diluted acetic acid and then treated with acetic anhydride. The *acetyl* derivative of base (β) separated, and crystallised from dilute acetic acid (charcoal) in small needles, m. p. 115—116° (Found : N, 5·2. $C_{16}H_{16}ONCl$ requires N, 5·1%). The hydrochloride of the α-base gave with ammmonia the *base* itself, small rhombohedra, m. p. 75—77°, from alcohol (Found : N, 6·5. $C_{14}H_{14}NCl$ requires N, 6·1%). The *acetyl* derivative of base α crystallised from alcohol or from aqueous alcohol in needles, m. p. 123—124° (Found : N, 5·2%). The m. p. of a mixture of the two acetyl derivatives was 90—105°. Recrystallisation of the hydrochloride of base α gave needles, m. p. 223—224° (decomp.).

Treatment of Nitro-2-chlorodimethyldiphenyl with Piperidine.—7·1160 G. of the crude nitration product were heated in a closed tube with excess of piperidine for 3 hours at 100°. A little alkali was added and then ether. The ethereal layer was separated and well washed with water. The united aqueous extracts were freed from ether, acidified with nitric acid, and treated with silver nitrate. The silver chloride obtained, after being washed with hot chloroform to remove traces of organic matter, weighed 0·0636 g., corresponding to elimination of chlorine from 1·6% of the nitration product.

The results of three typical series of experiments were as follows:

α-Base, weighed as hydrochloride.	β-Base, weighed as acetyl derivative.	Ratio β/α of free bases.
(1) Crude, 1·0 g.	2·92 g., m. p. 108—111°	2·8
Recryst., 0·75 g.	2·20 g., m. p. 114—115°	2·6
(2) Crude, 0·62 g.	1·82 g., m. p. 108—111°	2·9
(3) Recovered from piperidine treatment:		
Crude, 0·54 g.	1·36 g., m. p. 107—112°	2·6
Recryst., 0·40 g.	1·08 g., m. p. 114—116°	2·6

2 : 2′-*Dichloro*-4 - 4′-*dimethyldiphenyl.*—The base obtained by hydrolysis, with hot concentrated hydrochloric acid, of the above β-chloro-acetamido-derivative, was diazotised, and submitted to a Sandmeyer reaction. Distillation in steam gave the dichloro-compound, which crystallised from alcohol in small plates, m. p. 90°. It was identical with 2 : 2′-*dichloro*-4 : 4′-*dimethyldiphenyl*, prepared in a similar manner from 2 : 2′-diamino-4 : 4′-dimethyldiphenyl (Found: Cl, 28·3. $C_{14}H_{12}Cl_2$ requires Cl, 28·3%).

2-*Bromo*-4 : 4′-*dimethyldiphenyl.*—Direct bromination of dimethyldiphenyl with bromine (2 mols.) in acetic acid in presence of sodium acetate at the b. p., followed by addition of much water, led to a complex mixture of products. 4 : 4′-Dimethyldiphenyl-2-diazonium perbromide was therefore prepared in the usual way from the 2-amino-compound, and decomposed in hot alcohol. The alcohol was removed, and the residue washed with alkali. The dark oil deposited crystals of what appears to be a bromoethoxydimethyldiphenyl, m. p. 67—68° (Found: Br, 26·9. $C_{16}H_{17}OBr$ requires Br, 26·2%). Decomposition of the perbromide in hot glacial acetic acid gave a mixture of solid substances which proved to be the result of unwanted further bromination. The perbromide was finally decomposed by introducing it in small quantities into a flask kept at 100°. The residue was dissolved in carbon tetrachloride, and the solution washed with alkali, dried, and distilled three times at 12 mm. pressure. The 2-*bromo*-4 : 4′-*dimethyldiphenyl*, containing a small amount of a dibromo-compound, from which it could not be separated, had b. p. 183—187°/12 mm. (Found: Br, 32·8. $C_{14}H_{13}Br$ requires Br, 30·7%).

Application of the Sandmeyer reaction to 2-amino-4 : 4′-dimethyldiphenyl gave the 2-bromo-compound, b. p. 182—184°/18 mm., mixed with a small amount of ditolyl, from which it could not be separated (Found: Br, 28·9%).

Nitration of 2-Bromo-4 : 4′-dimethyldiphenyl.—The bromo-compound was nitrated in a manner similar to that described for the chloro-compound. Treatment with piperidine indicated the presence of 1·3% of labile bromine.

Reduction of Nitration Product.—The oily nitration product was reduced with stannous chloride as described under the chloro-series. Two basic substances, α and β, were obtained, representing 58—62% of the total reduction product, the remainder being insoluble in acid. The less soluble α-hydrochloride crystallised from hydrochloric acid in needles, m. p. 227—229° (decomp.). The free α-base was a gum, but its *acetyl* derivative crystallised from dilute acetic acid in needles, m. p. 146—147° (Found: N, 4·4. $C_{16}H_{16}ONBr$ requires N, 4·4%). The more soluble β-hydrochloride was a gum, but a small amount was obtained in minute hexagonal plates. The β-base was a gum, but its *acetyl* derivative crystallised from dilute acetic acid in clusters of small needles, m. p. 134—135° (Found: N, 4·7%). A mixture of the two acetyl derivatives melted at 120—132°.

The results of four typical series of experiments are as follows:

α-Base, weighed as hydrochloride.	β-Base, weighed as acetyl derivative.	Ratio, β/α, of free bases.
(1) Crude, 1·06 g.	1·90 g., m. p. 121—126°	1·8
Recryst., 0·90 g.	1·60 g., m. p. 132—134°	1·8
(2) Crude, 0·42 g.	0·70 g.	1·7
Recryst., 0·25 g.	0·45 g.	
(3) 0·60 g.	1·10 g.	1·8
(4) Recovered from piperidine treatment, etc., 0·47 g.	0·80 g., m. p. 132—134°, and 0·18 g., m. p. 124—126°	1·6

2 : 2′-*Dibromo*-4 : 4′-*dimethyldiphenyl*.—The gummy base obtained by hydrolysis with hydrochloric acid of the purified acetyl derivative of the β-base was submitted to a Sandmeyer reaction. The mixture was made alkaline and steam-distilled. The oil distilling later solidified, and crystallisation from alcohol gave the dibromo-compound, the m. p. of which was not depressed by admixture with the product, m. p. 114—115°, obtained from 2 : 2′-diamino-4 : 4′-dimethyldiphenyl by the Sandmeyer reaction. During the Carius determination of halogen in these two specimens, the tubes burst, and it was impracticable to prepare more of them. It was therefore not proved that the β-base was 2-bromo-2′-amino-4 : 4′-dimethyldiphenyl, but from the above evidence of m. p. and from the complete parallelism of the products of nitration, reduction, acetylation, etc., in this series with those in the chloro- and iodo-series (below), in which the β-bases were proved to be of the 2 : 2′-type, and also from the fact that the m. p.'s of the acetyl derivatives and hydrochlorides of the bromo-α- and -β-bases lie between those of the corresponding chloro- and iodo-compounds, it is extremely probable that the β-bromo-compounds are derived from the 2′-nitro-compound.

2-*Iodo*-4 : 4′-*dimethyldiphenyl*.—30 G. of 2-amino-4 : 4′-dimethyldiphenyl were suspended in 10 c.c. of concentrated sulphuric acid, diluted with 100 c.c. of water, cooled to 0°, and diazotised. Urea was added, and the solution was poured into an aqueous solution of 35 g. of potassium iodide and 60 g. of hydrated sodium acetate at 30°. The mixture was kept for an hour, warmed, and then distilled in steam. About 1·5 g. of ditolyl came over first, and was followed by an oil, which was manipulated by means of chloroform. It distilled at 198—208°/15 mm. (12 g.), and on redistillation at 200—205°/15 mm. The decomposed diazo-solution was alternatively extracted with carbon tetrachloride, and the latter with alkali. After removal of the carbon tetrachloride and cooling to − 20°, 3 g. of an azo-compound separated, and the mother-liquor was distilled. About 1 g. of ditolyl and 12·5 g. of oil, b. p. 200—210°/15 mm., were obtained, and redistillation, after previous treatment with mercury to remove free iodine, gave 11 g. of 2-*iodo*-4 : 4′-*dimethyldiphenyl*, b. p. 200—205°/15 mm. (Found : I, 40·8. $C_{14}H_{13}I$ requires I, 41·2%).

Nitration of 2-*Iodo*-4 : 4′-*dimethyldiphenyl*.—To the iodo-compound (1 mol.) were added cautiously, with shaking, 2 mols. of nitric acid (*d* 1·5) mixed with 1 vol. of glacial acetic acid. The mixture was heated at 100° for 10 minutes and then poured into excess of water. The reddish oil was worked up in the manner described for the chloro- and bromo-compounds, 98·5—99·7% of the theoretically possible mononitro-mixture resulting. Piperidine treatment indicated 1·4% of labile iodine in the total crude nitration product. Reduction was carried out as described for the chloro- and bromo-compounds. The acid-soluble part of the total reduction product (57—63%) led to two base hydrochlorides, α and β. The α-hydrochloride formed leaflets, m. p. 222—224° (decomp.), and the α-*acetyl* derivative crystallised from dilute acetic acid in small prisms, m. p. 165—166° (Found : N, 4·2. $C_{16}H_{16}ONI$ requires N, 3·9%). The *acetyl* derivative of the β-base crystallised from dilute acetic acid in needles, m. p. 160—161° (Found : N, 3·9%), or 140—152° when mixed with the α-acetyl derivative. Neither of the bases could be obtained crystalline.

The results of six typical series of experiments are as follows :

α-Base, weighed as hydrochloride.	β-Base, weighed as acetyl derivative.	Ratio, β/α, of free bases.
(1) Crude, 1·0 g.	2·2 g., m. p. 141—147°	2·2
Recryst., 0·6 g.	1·36 g., m. p. 158—160°	2·3
(2) *Recovered from piperidine treatment, etc.* :		
Crude, 0·61 g.	1·35 g., m. p. 140—146°	2·2
Recryst., 0·40 g.	0·91 g., m. p. 159—160°	2·3
(3) 0·36 g.	0·86 g.	2·4
(4) 0·65 g.	1·55 g.	2·4
(5) 0·55 g.	1·10 g.	2·0
(6) 0·45 g.	0·91 g.	2·1

2 : 2′-*Di-iodo*-4 : 4′-*dimethyldiphenyl*.—The base obtained by hydrolysis with hot concentrated hydrochloric acid, containing a little alcohol, of the β-acetyl derivative above was diazotised in hydrochloric acid and the solution was poured into potassium iodide solution. When decomposition was complete in the warm, the product was steam-distilled. The colourless product crystallised from methyl alcohol in large hexagonal plates, m. p. 116—117° (0·4 g. from 2·6 g. of acetamido-compound), and was identical with 2 : 2′-*di-iodo*-4 : 4′-*dimethyldiphenyl* similarly prepared from 2 : 2′-diaminoditolyl (Found : I, 58·4. $C_{14}H_{12}I_2$ requires I, 58·5%). A yellow insoluble powder, which was the main product of the diazo-reaction, was ditolyleneiodonium iodide (cf. Angelletti and Brambilla, *loc. cit.*). This was heated at 240°, and gave a sublimate, m. p. 113°, melting at 115—116° when mixed with the above di-iodo-compound.

2-Hydroxy-4 : 4'-dimethyldiphenyl.—This compound was formed in the preparation of all the 2-halogeno-compounds, from which it was separated by usual methods. It was also prepared, in 60% yield, by heating an aqueous solution of 4 : 4'-dimethyldiphenyl-2-diazonium sulphate. After filtration of the resulting suspension, acid was added, the *hydroxy*-compound then separating; it crystallised from aqueous alcohol in fine needles, m. p. 57—58°, having a floral odour (Found : C, 84·6; H, 7·1. $C_{14}H_{14}O$ requires C, 84·8; H, 7·1%). The *p*-toluenesulphonate formed long needles, m. p. 130°.

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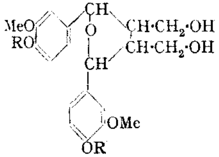
UNIVERSITY OF LONDON (BEDFORD COLLEGE). [*Received, November 28th,* 1936.]

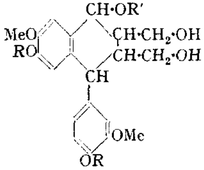
53. *The Resinol of* Olea Cunninghamii (*Maire*).

By LINDSAY H. BRIGGS and A. G. FRIEBERG.

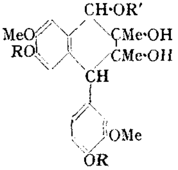
THE crystalline resin occasionally found in the heart shakes of *Olea Cunninghamii* (Maori name Maire) has been identified as *iso*olivil : this is the first record of the occurrence of the substance in nature. Hitherto it has only been obtained by the action of warm dilute acetic or formic acid on olivil, from the oleo-resin of *Olea Europoca* (Körner and Vanzetti, *Atti R. Accad. Lincei*, 1903, **12**, 122). From the investigations of Vanzetti and co-workers (Körner and Vanzetti, *Mem. R. Accad. Lincei*, 1911, **8**, 749; Vanzetti, *Monatsh.*, 1929, **52**, 163; *Gazzetta*, 1929, **59**, 373; *Atti R. Accad. Lincei*, 1934, **19**, 421; Vanzetti and Dreyfuss, *Gazzetta*, 1934, **64**, 381) the formulæ (I; R = H) and (II; R, R' = H) have been proposed for olivil and *iso*olivil respectively.



(I.)



(II.)



(III.)

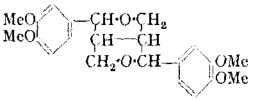
At the beginning of the present investigation there was no definite proof of the constitution of these resinols : the carbon skeleton was probable from chemical and phytochemical considerations, but the nature and position of the three alcoholic groups of *iso*olivil were unknown, because no derivatives of these groups had been recorded. Since the completion of this work, Dreyfuss (*Gazzetta*, 1936, **66**, 96) has oxidised *iso*olivil dimethyl ether to the lactone of 6 : 7-dimethoxy-1-(3' : 4'-dimethoxyphenyl)-3-hydroxymethylnaphthalene-2-carboxylic acid, identical with that synthesised by Haworth and Sheldrick (J., 1935, 636), thus confirming the carbon skeleton of *iso*olivil. The position of the alcoholic groups in (II) is supported by the present investigation.

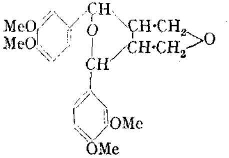
The *iso*olivil has been identified by its properties, the preparation of dimethyl and diethyl ethers, and by the oxidation of the dimethyl ether to 4 : 5-dimethoxy-2-(3' : 4'-dimethoxyphenyl)phthalide. The diethyl ether was obtained in almost theoretical yield by the action of ethyl sulphate and alkali, but much poorer yields of the dimethyl ether were obtained by similar methods. From methylations with excess of methyl sulphate a *trimethyl* ether was obtained as a by-product, which, from the known facility of methylation of benzyl alcohol, is probably (II; R, R' = CH_3). It still contains two active hydrogen atoms (Zerewitinoff estimation), but was recovered mostly unchanged after attempts to benzoylate it and to form the acid phthalate under conditions usually suitable for primary alcohols. From this failure to obtain derivatives, another formula (III; R, R' = H) was considered for *iso*-

olivil, also based on the symmetrical formula of olivil but containing two tertiary instead of two primary alcoholic groups. A substance of this formula should be easily dehydrated, but, although such products were obtained with various reagents, they were amorphous in each case. The trimethyl ether, however, distils unchanged at 0·04 mm., and further evidence against (III) was provided by a *C*-alkyl determination kindly carried out by Dr. H. Roth of Heidelberg, who obtained a negative result.

An attempt was made to obtain proof of the carbon skeleton by a method used with success in the podophyllotoxin series, *viz.*, demethylation, followed by zinc dust distillation (Borsche and Niemann, *Annalen*, 1932, **484**, 126; 1933, **499**, 59), but the only product, isolated in small yield, was pyrocatechol.

Erdtmann (*Svensk Kem. Tidskr.*, 1934, **46**, 229; *Annalen*, 1935, **516**, 162), in discussing the structure of pinoresinol dimethyl ether (cf. Bamberger, *Monatsh.*, 1894, **15**, 505; 1897, **18**, 481; Bamberger and Vischner, *ibid.*, 1900, **21**, 949; Bamberger and von Kleimburg, *ibid.*, 1917, **38**, 457), enantiomorphous with eudesmin (Robinson and Smith, *J. Roy. Soc. N. S. Wales*, 1914, **48**, 449), prefers formula (IV) to the alternative one (V), suggested among others by Robinson and Smith (*loc. cit.*), which only differs from that of olivil dimethyl

(IV.) 

 (V.)

ether by the closing of an additional hydrofuran ring, on the ground that, unlike olivil, these resinols do not undergo ring closure to a phenylnaphthalene. Formula (V) is, however, equally consistent with the reactions of these resinols and is better supported by phytochemical considerations; failure to isomerise may be due to the stability of the two tetrahydrofuran nuclei, and additional support is given by the fact that the dimethyl and diethyl ethers of olivil are not isomerised (Körner and Vanzetti, *loc. cit.*).

Experimental.

Olea Cunninghamii, one of four species of *Oleaceae* endemic to New Zealand, is a lofty evergreen tree restricted to the North Island.

The resin scrapings and wood chips were extracted with boiling alcohol and concentrated. On the addition of ether, the resinol crystallised in elongated rhombs; it was further purified from alcohol–ether and acetone. The pure substance is neutral in reaction, insoluble in sodium bicarbonate, but soluble in sodium hydroxide solution, freely soluble in methyl and ethyl alcohols, glacial acetic acid and pyridine and insoluble in water, ether, light petroleum, benzene and chloroform. It gives a bright green coloration with alcoholic ferric chloride, a violet coloration with concentrated sulphuric acid, and reduces Tollens' reagent. The crystals from alcohol–ether melt at *ca.* 98°, but after standing in the air for some days melt at 163—164°, $[\alpha]_D^{24°} + 61·8°$ (absolute alcohol); Vanzetti records m. p. 167°, $[\alpha]_D^{25°} + 61·1°$ (alcohol). No further loss occurs on drying in a vacuum. When recrystallised from acetone, they melt indefinitely at *ca.* 100°, but after exposure to air for a similar period contract at 144° and melt at 163—164°. In this case the air-dried crystals lose further weight on drying in a vacuum at room temperature [Found in material freshly recrystallised from alcohol–ether: *M* (ebullioscopic in acetone), 435; loss on drying in air for 1 month, 9·6%. Found in air-dried sample: C, 62·2; H, 6·3. Calc. for $C_{20}H_{24}O_7,C_2H_5{\cdot}OH,\frac{1}{2}H_2O$: *M*, 431; loss of $C_2H_5{\cdot}OH$, 10·7%. Calc. for $C_{20}H_{24}O_7,\frac{1}{2}H_2O$: C, 62·3; H, 6·5%. Found in sample recrystallised from acetone: loss on drying in air, 12·6%; further loss on drying in a vacuum at room temperature, 2·9%. Found in air-dried sample: C, 60·6; H, 6·5. Found in sample dried at 110°/high vacuum: C, 63·5; H, 6·5; *M* (Rast), 379. Calc. for $C_{20}H_{24}O_7,C_3H_6O,H_2O$: for loss of C_3H_6O, 12·8%. Calc. for $C_{20}H_{24}O_7,H_2O$: C, 60·9; H, 6·6; loss of H_2O, 4·7%. Calc. for $C_{20}H_{24}O_7$: C, 63·8; H, 6·4%; *M*, 376).

Methylation of iso*Olivil*.—The dimethyl ether, obtained in the usual way with methyl sulphate and alkali, crystallised from methyl alcohol in needles, m. p. 181—181·5°, $[\alpha]_D^{20°} + 46·6°$ (alcohol)

(lit., m. p. 184·5°, $[\alpha]_D^{20\cdot5°}$ + 33·58°). The yield with molecular proportions was 40%, and was increased to 60% with double quantities (Found : C, 64·8, 65·1 ; H, 6·9, 7·1. Calc. for $C_{22}H_{26}O_7$: C, 65·3 ; H, 6·9%). With 7 mols. of methyl sulphate or more, the dimethyl ether was obtained and a gummy residual product which after successive crystallisations from water and chloroform–light petroleum formed needles, m. p. 153—154°, and distilled at 0·04 mm. (temperature of bath 280°). The distilled product was a colourless glass, m. p. 55—65°, which after crystallisation from water, methyl alcohol and chloroform–light petroleum had the original m. p. 153—154°, $[\alpha]_D^{17°}$ + 26·23° (chloroform) [Found in distilled product : C, 66·0 ; H, 7·3 ; OMe, 37·5 ; OH (Zerewitinoff estimation in dioxan), 11·4. Found in crystalline product : C, 65·7 ; H, 7·3. $C_{23}H_{30}O_7$ requires C, 66·0 ; H, 7·2 ; OMe, 37·1 ; OH, 9·0%].

*iso*Olivil *trimethyl ether* (0·2 g.), dissolved in dry benzene (2 c.c.), was heated with phthalic anhydride (0·15 g.) at 100° for 1½ hours. After removal of the benzene by evaporation the product was triturated with ether. The insoluble residue (0·15 g.) crystallised from methyl alcohol in needles, m. p. 153—153·5°, undepressed by the initial material.

Oxidation of iso*Olivil Dimethyl Ether.*—To a mechanically stirred suspension of the dimethyl ether (2 g.) in 25 c.c. of 10% sodium hydroxide solution at 100° was gradually added (1½ hours) a solution of potassium permanganate (5·5 g.) in water (200 c.c.). The amorphous product obtained after passage of sulphur dioxide and standing for 2 days was dissolved in sodium hydroxide solution and reprecipitated with sulphur dioxide. After repeated crystallisations from alcohol and finally from methyl alcohol it had m. p. 186—187°. 4 : 5-Dimethoxy-2-(3′ : 4′-dimethoxyphenyl)phthalide has m. p. 188° (Vanzetti and Dreyfuss, *loc. cit.*). Other products were obtained but were not investigated.

Degradation of iso*Olivil.*—*iso*Olivil (5 g.) in glacial acetic acid solution (50 c.c.) was demethylated with hydriodic acid (20 c.c.) and the acids were removed by distillation in a vacuum. The residue was taken up in ether, washed with sodium thiosulphate solution, mixed with zinc dust, and after removal of ether distilled at 0·04 mm. The only product was a crystalline sublimate (0·1 g.), m. p. 101°, giving the characteristic colour reaction of pyrocatechol, an authentic specimen of which did not depress the melting point.

Diethyl Ether.—This, obtained in theoretical yield by means of ethyl sulphate and alkali, formed needles from alcohol, m. p. 178—178·5°, $[\alpha]_D^{15°}$ + 46·05° (alcohol) (Found : C, 66·5 ; H, 7·5. Calc. for $C_{24}H_{32}O_7$: C, 66·7 ; H, 7·4%). Vanzetti gives m. p. 179—179·5° and $[\alpha]_D^{23\cdot5°}$ + 38·22° (alcohol).

We are indebted to Mr. J. Holt for the raw material used in this research, to the Chemical Society for a grant, and to the Royal Society of New Zealand for the loan of apparatus.

Auckland University College,
Auckland, New Zealand. [*Received, September 29th*, 1936.]

54. *The Temperature Coefficient of the Thermal Decomposition of Silver Oxalate.*

By James Y. Macdonald.

Benton and Cunningham, studying the decomposition of silver oxalate (*J. Amer. Chem. Soc.*, 1935, **57**, 2227), claimed to have evidence that the energy of activation of the formation of nuclei was much greater than that of the rate of propagation of decomposition through the crystals. This would mean an increase in the temperature coefficient of the whole reaction at low temperatures, since its course would be governed by the relatively slow rate of formation of nuclei. At higher temperatures, the rate of spreading of decomposition from nuclei would become the "slow" reaction which would control the form of the reaction as a whole. The figure which they give, *viz.*, 64,000 cals., is equivalent to a temperature coefficient of 11·0 in the range 80—110°, and in support of this they quote experiments in which they were unable to detect any reaction during 13½ hours at 80°. On the other hand, the author (J., 1936, 839) showed that their calculation was erroneous, and found that the over-all temperature coefficient of the reaction was about 3·0, and that it was constant over the more limited range examined. Unfortunately, his experiments at the lowest temperature (85°) had to be curtailed for technical reasons, and were not considered

sufficiently trustworthy to quote. In order to settle the point, two complete runs have now been made at 80°, and these are compared below with runs with the same specimen at 110° and 130°. It will be seen that all the characteristics of the reaction are maintained at the low temperature, and that a coefficient of about 3·0 was obtained, in agreement with the author's earlier results.

EXPERIMENTAL.

The specimen used (*R*) had been prepared about 1931 in complete darkness, and had never been exposed to light. The initial rate of decomposition was found to be rather high, in accordance with the assumption that slight decomposition had taken place at room temperature, and calculation showed that this was of the right order of magnitude for a temperature of 18°, a time of 5 years, and a coefficient of 3·0. The specimen had been prepared with an excess of sodium oxalate, and was therefore of the more unstable type. Its rate of decomposition was measured exactly as described by the author (J., 1936, 832), and the two runs at 80° were conducted simultaneously, the same thermostat and the same vacuum backing being used.

In the following table, cols. 2—5 give the times (in mins.) taken by the various samples to attain the degree of decomposition given in col. 1. These figures were obtained by integrating the rate–time graphs, as already described (*loc. cit.*). Cols. 6 and 7 give, respectively, the temperature coefficient between 80° and 110° (the mean of the two experiments at 80° being used) and that between 110° and 130°. The coefficients are worked out for each percentage decomposition, and their constancy shows that the shape of the graphs is independent of temperature.

Decomptn., %.	80°.	80°.	110°.	130°.	Coeff., 80—110°.	Coeff., 110—130°.
5	1850	1850	94·0	8·0	2·70	3·42
10	2500	2460	124·1	11·1	2·71	3·34
20	3360	3200	156·0	14·5	2·76	3·27
30	3660	3910	179·0	16·9	2·76	3·28
40	4070	4330	197·6	18·4	2·76	3·26
50	4430	4750	214·0	20·4	2·78	3·24
60	4850	5210	231·0	22·0	2·79	3·24
70	5350	5710	249·8	23·9	2·81	3·22
80	5910	6300	270·5	26·0	2·83	3·22
90	6660	7090	303·0	29·7	2·83	3·19
					Mean 2·77	3·27

The second table gives the values of a and p in the equation $dx/dt = ae^{pt}$ [*loc. cit.*, p. 843, equation (3)], and these may be compared with the values for other specimens given in that paper. In the present case, the figures are not very reliable, because the logarithmic graphs from which they are obtained show considerable curvature.

	80°.	110°.	130°.	Coeff.
$a \times 10^8$	0·358	11·0	90·8	3·03
$p \times 10^4$	0·0987	1·82	20·6	2·87

UNITED COLLEGE, ST. ANDREWS. [*Received, November 18th, 1936.*]

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55. *Optical Activity dependent on Restricted Rotation in a Benzene Derivative.*

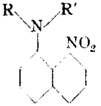
By WILLIAM H. MILLS and RAYMOND M. KELHAM.

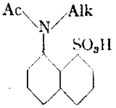
AFTER the molecular dissymmetry of substitution derivatives of diphenyl, discovered by Kenner and Christie (J., 1922, **121**, 614), had been interpreted as a consequence of the restrictive effect of the substituent groups on the relative rotation of the two benzene nuclei in the diphenyl molecule, it was shown by one of us and Elliott (J., 1928, 1292) that *peri*-disubstituted derivatives of naphthalene could exhibit an analogous phenomenon.

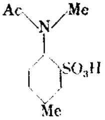
Proof of this was given by obtaining a compound of the type (I) in optically active forms. In this compound the optical activity arose from the restriction of the rotation of a disubstituted α-amino-group, R–N–R′, about the nitrogen–naphthyl valency bond, the restriction being effected by the nitro-group in the adjacent *peri*-position.

It is shown in the present communication that optical activity can be produced in a similar way in the benzene series. The rotation of a disubstituted amino-group attached to

a benzene nucleus can be restricted by a substituent in the ortho-position so as to give rise to molecular dissymmetry of considerable persistence.

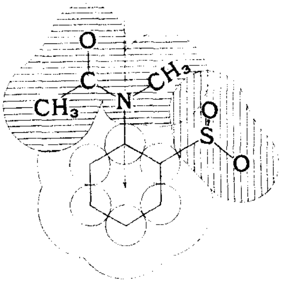

(I.)


(II.)


(III.)

An investigation carried out in this laboratory by one of us with P. J. Garner and S. Marriage, the results of which will shortly be communicated, has shown that substitution derivatives of 1-naphthylamine-8-sulphonic acid of the type (II) (in which Alk represents an alkyl group and Ac an acyl group) can be obtained, like the nitro-compound (I), in optically active forms.

The rates of racemisation of a number of these *peri*-compounds were measured, and found to vary greatly with the nature of the acyl substituent Ac. The acetylmethyl derivative, in particular, possessed so high a degree of optical stability that we were led to make a similar investigation of an analogously constituted ortho-compound of the benzene series.



We accordingly prepared and studied *N*-acetyl-*N*-methyl-*p*-toluidine-3-sulphonic acid (III) and found that the salts of this compound could, in fact, be obtained in an optically active form. The dextrorotatory modification was obtained by means of brucine. The *brucine* salt showed mutarotation when dissolved in chloroform, the repeatedly re-crystallised compound giving in chloroform solution an initial specific rotation $[\alpha]_{5461} + 2{\cdot}4°$, which gradually fell, according to the unimolecular law, to an equilibrium value of $-5{\cdot}8°$ with a half-change period, at 16·7°, of 2·8 hours.

The disappearance of dextrorotation shown in the mutarotation indicated that in this salt the brucine was combined with an optically labile dextrorotatory form of the acid. This was confirmed by converting the brucine salt into the *sodium* salt by treatment in chloroform solution with an alcoholic solution of sodium ethoxide. The sodium salt precipitated had the composition $C_6H_3Me(NMeAc){\cdot}SO_3Na,2H_2O$ and was dextrorotatory. It showed an initial specific rotation $[\alpha]_{5461}$ of $+ 6{\cdot}06°$, which gradually fell to zero, the half-change period at 16·6° being 5·25 hours.

The rates of racemisation of the sodium salt in aqueous solution were measured at four different temperatures ranging from 16·6° to 35°, and the corresponding values of the unimolecular reaction velocity constant k (time in minutes) are given in the following table :

t.	16·6°.	24°.	28°.	35°.
k(found)	0·0022	0·0055	0·0097	0·022
k(calc.)	0·0021	0·0057	0·0095	0·022

The critical energy increment for the racemisation, calculated from the slope of the $\log_e k$–$1/T$ curve, is 22·6 kg.-cals. The values given for k(calc.) are those calculated from the Arrhenius equation $k = \chi e^{-E/RT}$, the values $2{\cdot}797 \times 10^{14}$ and 22,613 being used for the constants χ and E. These values give the best straight line through the points representing the values found for k at the four temperatures on the $\log_e k$–$1/T$ diagram, and the differences between k(found) and k(calc.) serve to indicate the order of magnitude of the experimental errors of the determinations.

The figure, which is a scale drawing of the essential parts of the molecule of the acid, gives

an approximate idea of the probable amount of overlap of the *N*-methyl- and the *N*-acetyl-group with the SO_3-group. It is based on the following values (in A.) of the dimensions concerned: *internuclear distances*, $C_{Ar.}$–$C_{Al.}$ 1·39, $C_{Ar.}$–S 1·82, S–O 1·50, $C_{Ar.}$–N 1·44, $C_{Al.}$–N 1·48; *external radii* (based on the distances of closest approach observed in crystals), CH_2 1·6, O 1·33.

The overlap of the groups must evidently be smaller when they occupy two *o*-positions in benzene than when they are in two *peri*-positions in naphthalene, and the critical increment of energy for racemisation is, in fact, less for the benzene derivative (22·6 kg.-cals.) than had been found for the corresponding naphthalene derivative (26·9 kg.-cals.).

The brucine salt of *N*-acetyl-*N*-methylanthranilic acid was also examined. This acid contains a carboxyl in place of the sulphonic group of the compound (III), but since no permanent overlap of the Me–N–Ac grouping and a carboxyl in the *o*-position is to be anticipated, it should not be capable of showing optical activity, and, in fact, its brucine salt gave no sign of mutarotation.

EXPERIMENTAL.

N-Acetyl-N-methyl-p-toluidine (compare Thielepape, *Ber.*, 1935, **68**, 751).—Finely granulated sodium (12 g.) is added to a solution of perfectly dry aceto-*p*-toluidide (80 g.) in benzene (600 c.c.), and the mixture heated on a water-bath with frequent shaking. The sodium dissolves slowly (2—2½ hrs.) to give a white semi-solid mass of sodioacet-*p*-toluidide. Methyl sulphate (68 g.) is then slowly added, and after the initial vigorous reaction has subsided, the heating on the water-bath is continued for a further 1½ hours. Water (300 c.c.) is added to dissolve sodium sulphate present as a gel, and the benzene layer separated, dried over calcium chloride, and concentrated to about 100 c.c. *N*-Acetyl-*N*-methyl-*p*-toluidine crystallises (m. p. 80°), and is sufficiently pure for the following stage.

Sodium N-Methyl-p-toluidine-3-sulphonate.—*N*-Acetyl-*N*-methyl-*p*-toluidine (16 g.) is treated with concentrated sulphuric acid (13 g.) with the addition of ammonium vanadate (0·2 g.) as catalyst. The mixture is mechanically stirred under reduced pressure (20 mm.), the reaction vessel being maintained at 170—180° in an oil-bath. Sulphonation and elimination of the *N*-acetyl radical take place together, and the process is complete when acetic acid ceases to distil from the reaction vessel (about 2 hrs.). The hot liquid mass of crude *N*-methyl-*p*-toluidine-3-sulphonic acid is poured into water (300 c.c.), the liquid made alkaline with sodium hydroxide, and steam-distilled to remove unsulphonated *N*-methyl-*p*-toluidine. The resulting solution of sodium *N*-methyl-*p*-toluidine-3-sulphonate, after decolorisation with animal charcoal and concentration, deposits the pure salt (16·5 g.) on cooling.

Sodium N-Acetyl-N-methyl-p-toluidine-3-sulphonate.—Dry sodium *N*-methyl-*p*-toluidine-3-sulphonate (11 g.) is treated with twice the theoretical quantity of acetic anhydride (5 g.) and heated on a water-bath for 1 hour with occasional shaking. The cold product is powdered, and freed from unchanged acetic anhydride by extraction with ether in a Soxhlet apparatus. The crude material is finally crystallised twice from small quantities of ethyl alcohol. The pure *sodium N-acetyl-N-methyl-p-toluidine-3-sulphonate dihydrate* melts at 81—82°, and the *anhydrous* salt at 277—279° with darkening (Found: H_2O, 12·4. $C_{10}H_{12}O_4NSNa,2H_2O$ requires H_2O, 12·0%. Found, for anhydrous salt: N, 5·3; S, 12·1; Na, 8·8. $C_{10}H_{12}O_4NSNa$ requires N, 5·3; S, 12·1; Na, 8·7%).

Brucine N-Acetyl-N-methyl-p-toluidine-3-sulphonate.—A cold solution of brucine acetate (22·7 g.) in water (400 c.c.) was mixed with a cold solution of sodium *N*-acetyl-*N*-methyl-*p*-toluidine-3-sulphonate dihydrate (15·05 g.) in water (400 c.c.). After standing overnight, the *brucine* salt crystallised (16·5 g.), and concentration of the mother-liquor over concentrated sulphuric acid in a vacuum gave a further quantity (18 g.) (Found: C, 58·4; H, 6·5; N, 6·3; H_2O, 5·6. $C_{33}H_{39}O_8N_3S,2H_2O$ requires C, 58·8; H, 6·4; N, 6·3; H_2O, 5·4%). The brucine salt was recrystallised from warm water (60°), and a portion was dehydrated in a vacuum over phosphoric oxide and examined for mutarotation in chloroform solution: 0·44 g. of the salt in 30 c.c. ($l = 4$) gave $[\alpha]_{5461}$ − 0·56°, falling to − 0·86°, the corresponding values of $[\alpha]_{5461}^{17°}$ being − 9·55° and − 14·67°, with mean value of $k = 0·0044$.

The brucine salt (75 g.) was then recrystallised from water eight times, each fraction being examined polarimetrically. A portion (0·3389 g.) of the eighth fraction (total 12 g.) in chloroform solution (25 c.c.; $l = 4$; $t = 16·7°$) gave the following results:

Time (mins.).	α_{5461}.*	$[\alpha]_{5461}$.	k.	Time (mins.).	α_{5461}.*	$[\alpha]_{5461}$.	k.
0	+0·131	+2·43	—	110	−0·156	−2·89	0·0041
5	+0·108	+2·0	0·0046	170	−0·202	−3·74	0·0035
10	+0·078	+1·45	0·0044	245	−0·247	−4·58	0·0034
25	+0·028	+0·52	0·0046	425	−0·300	−5·55	0·0035
65	−0·090	−1·66	0·0046	∞	−0·314	−5·81	—

Mean value of k = 0·0041, time of half-change = 169 mins.

* The values of α are each the mean of six readings, three taken before and three taken after the recorded times.

This purified brucine salt was used to prepare the optically active sodium salt, but we have no evidence that the resolution had been carried to completion.

d-*Sodium* N-*Acetyl*-N-*methyl*-p-*toluidine-3-sulphonate.*—To a solution of the purified brucine salt (4·244 g.) in chloroform (8 c.c.), a solution of sodium ethoxide in alcohol (0·1537 g. Na in 1·5 c.c. 90% ethyl alcohol) was added. The mixture was then strongly cooled in a freezing mixture, and after scratching (2 mins.), the optically active hydrated *sodium* salt of *N*-acetyl-*N*-methyl-*p*-toluidine-3-sulphonic acid crystallised (1·19 g.). It was collected and washed with chloroform (Found : Na, 8·7; S, 12·2. $C_{10}H_{12}O_4NSNa$ requires Na, 8·7; S, 12·1%).

The following table gives the results of a series of observations of α_{5461} made at 16·6° on an aqueous solution of the sodium salt thus obtained (c = 1·928; l = 4).

Time, mins.	α_{5461}, obs.	calc.	Time, mins.	α_{5461}, obs.	calc.	Time, mins.	α_{5461}, obs.	calc.	Time, mins.	α_{5461}, obs.	calc.
0	0·47°	0·46°	50	0·41°	0·41°	175	0·315°	0·31°	360	0·21°	0·21°
5	0·46	0·45	80	0·38	0·38	210	0·29	0·29	450	0·18	0·17
15	0·45	0·44	115	0·36	0·36	270	0·25	0·25	475	0·16	0·16
30	0·43	0·43	135	0·345	0·34						

The mean value of the unimolecular reaction velocity constant k calculated from the natural logarithms of the observed rotations and the times of observation by Campbell's method (*Phil. Mag.*, 1924, **47**, 816) was 0·00220. The numbers given for α, calc., were calculated by using this value of k, and their close agreement with the experimental observations shows that the racemisation follows the unimolecular law. The specific rotation $[\alpha]_{5461}$ calculated from the first observation was + 6·06°.

The later stages of the racemisation are not recorded in the foregoing table, since the rotations became too small to be measured with sufficient accuracy for use in the determination of k. Examined on the following day, the solution was found to have become completely inactive.

Critical Energy Increment for the Racemisation.—Observations of the rate of racemisation of the dextrorotatory sodium salt, similar to those made at 16·6°, were made at 24°, 28°, and 35°, and the results are recorded in the following tables. The unimolecular reaction velocity constants

Time, mins.	α_{5461}, obs.	calc.	Time, mins.	α_{5461}, obs.	calc.	Time, mins.	α_{5461}, obs.	calc.	Time, mins.	α_{5461}, obs.	calc.
				Racemisation at 24° (c = 1·820 ; l = 4).							
0	0·35°	0·35°	20	0·31°	0·31°	50	0·265°	0·26°	115	0·18°	0·18°
5	0·34	0·34	25	0·30	0·30	65	0·25	0·24	140	0·16	0·16
11	0·32	0·33	30	0·295	0·29	80	0·23	0·22	175	0·13	0·13
16	0·31	0·32	40	0·28	0·28	90	0·205	0·21	210	0·11	0·11
				$[\alpha]_{5461}$ (initial) = 4·83°; k(found) = 0·00553.							
				Racemisation at 28° (c = 1·768 ; l = 4).							
0	0·44	0·45	13	0·40	0·39	35·5	0·31	0·32	68	0·23	0·23
5	0·43	0·43	17	0·39	0·38	43	0·29	0·30	88	0·20	0·19
8	0·42	0·42	22	0·365	0·365	55	0·26	0·26	118	0·15	0·14
10	0·42	0·41	28	0·35	0·34						
				$[\alpha]_{5461}$ (initial) = 6·03°; k(found) = 0·00969.							
				Racemisation at 35° (c = 1·928 ; l = 4).							
0	0·50	0·50	16	0·37	0·36	30	0·26	0·26	70	0·11	0·11
5	0·45	0·46	19	0·33	0·34	35	0·235	0·24	90	0·07	0·07
8	0·42	0·43	22	0·31	0·31	45	0·20	0·19	120	0·03	0·04
12	0·40	0·39	26	0·29	0·29	55	0·15	0·15	160	0·015	0·015
				$[\alpha]_{5461}$ (initial) = 7·49°; k(found) = 0·02198.							

k were calculated as described for the observations made at 16·6°, and the values given for *k*(calc.) were obtained as there explained. In each case it was verified that the solutions finally became optically inactive. The solution kept at 35° ceased to show detectable activity after 8½ hours.

The critical increment of energy for the racemisation at all four temperatures was calculated as described on p. 275.

We are indebted to the Department of Scientific and Industrial Research, and to Pembroke College, for maintenance grants to one of us (R. M. K.).

UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, December 15th, 1936.*]

56. *Experiments on the Synthesis of Rotenone and its Derivatives. Part XI. Tetrahydrotubanol.*

By ALEXANDER ROBERTSON and T. S. SUBRAMANIAM.

ALTHOUGH the synthesis of tetrahydrotubanol (Haller, *J. Amer. Chem. Soc.*, 1933, **55**, 3032; Robertson, Part IV, J., 1933, 1164) serves to establish its constitution, the procedure is somewhat tedious and consequently we have investigated other possible, more convenient, routes to this compound. The following constitutes an improvement upon the older method. Application of the Fries reaction to the *iso*valerate of 7-hydroxy-4-methylcoumarin gave the isomeric *7-hydroxy-8-*iso*valeryl-4-methylcoumarin*, which on scission according to Baker's procedure (J., 1935, 631) furnished *2 : 6-dihydroxy*iso*valerophenone*, the orientation of which follows from its conversion into tetrahydrotubanol by reduction according to Clemmensen's method.

*7-Hydroxy-8-*iso*valeryl-4-methylcoumarin.*—Interaction of 7-hydroxy-4-methylcoumarin (8 g.) and *iso*valeryl chloride (6·5 g.) in pyridine (20 c.c.) during ½ hour gave rise to the *iso*valeric ester of 7-hydroxy-4-methylcoumarin, which separated from alcohol in colourless prisms (8·5 g.), m. p. 63—64°.

For the preparation of the keto-coumarin the following directions must be strictly adhered to. A flask containing an intimate mixture of the ester (10 g.) and well-powdered aluminium chloride (25 g.), protected from atmospheric moisture (calcium chloride tube), was placed in an oil-bath at 80° and heated to 85° in the course of 15 minutes. When the mild reaction (evolution of hydrogen chloride) had almost subsided (5 minutes later), the oil-bath was heated to 150° in the course of ¾ hour; temperature after ½ hour, 130°. After cooling, the *product* (3·3 g.) was isolated with the aid of ice and dilute hydrochloric acid in the usual manner; it crystallised from 50% alcohol in colourless, elongated, flat prisms, m. p. 109—110°, which give a bright purple coloration with alcoholic ferric chloride (Found: C, 69·5; H, 6·5. $C_{15}H_{16}O_4$ requires C, 69·2; H, 6·2%). Prepared according to the directions of Sun and Sah (*Amer. Chem. Abs.*, 1935, **29**, 466), the *o-chlorobenzoylhydrazone* separated from aqueous alcohol in colourless needles, m. p. 128—130° (decomp.) (Found: N, 7·0. $C_{22}H_{21}O_4N_2Cl$ requires N, 6·8%). The highly insoluble semicarbazone could not be purified.

Although Rây and co-workers (J., 1935, 814) report indications of the formation of 7-hydroxy-6-acetyl-4-methylcoumarin from 7-acetoxy-4-methylcoumarin, we have not been able to isolate an isomeric keto-coumarin in the present instance. Attempts to improve the yield of the keto-compound were unsuccessful.

*2 : 6-Dihydroxy*iso*valerophenone.*—The foregoing coumarin (8 g.) was refluxed with 20% aqueous sodium hydroxide (56 c.c.) in nitrogen for 3 hours and the mixture was cooled, acidified with hydrochloric acid, and extracted several times with ether. The combined extracts were washed with aqueous sodium bicarbonate to remove acidic material, dried, and evaporated, leaving the *ketone*, which separated from benzene-light petroleum (b. p. 60—80°) in pale yellow plates (4·5 g.), m. p. 67—68° (Found: C, 68·2; H, 7·2. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·2%). With alcoholic ferric chloride this compound gives a bluish-green coloration.

*2 : 6-Dihydroxy*iso*amylbenzene* (*Tetrahydrotubanol*).—Reduction of the foregoing ketone (4 g.) was effected by zinc amalgam in a boiling mixture of concentrated hydrochloric acid (25 c.c.), acetic acid (2 c.c.), and water (5 c.c.) in the course of 5 hours. On isolation with ether

the resulting tetrahydrotubanol (2·7 g.) was purified by distillation in a vacuum, b. p. 155—160°/22 mm., and then by recrystallisation from light petroleum (b. p. 60—80°), forming colourless needles, m. p. 83—84°, undepressed by admixture with an authentic specimen (Found: C, 73·4; H, 8·9. Calc. for $C_{11}H_{14}O_2$: C, 73·3; H, 8·9%).

UNIVERSITY OF LIVERPOOL. [*Received, December 18th, 1936.*]

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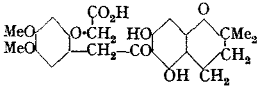
57. *Experiments on the Synthesis of Rotenone and its Derivatives. Part XII. The 2 : 2-Dimethyl-Δ^3-chromen Residue of Toxicarol.*

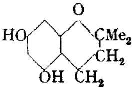
By WALTER BRIDGE, REGINALD G. HEYES, and ALEXANDER ROBERTSON.

IN Part V (J., 1935, 681) the structure of *apo-* and of dehydro*apo*-toxicarol was clearly demonstrated and the view was expressed that toxicarol and certain of its derivatives contain a 2 : 2-dimethyl-Δ^3-chromen nucleus involving the phloroglucinol residue, analogous to that obtaining in deguelin and tephrosin (Part II, J., 1932, 1380). This suggestion was based mainly on the production of acetone from toxicarol and deguelin by hydrolytic fission, in conjunction with the fact that, compared with toxicarol, coumarones and coumarans, *e.g.*, tubanol and *iso*tubanol, are relatively stable to hot aqueous sodium hydroxide, and before directing attention to the remaining experimental details required for the complete structure of toxicarol it was considered essential that clear evidence of the presence of the chromen residue should be obtained. In the first instance the oxidation of *O*-acetyldihydrodehydrotoxicarol was studied because it appeared reasonable to expect that, if toxicarol contained the 2 : 2-dimethyl-Δ^3-chromen system, it would probably give rise to an acid analogous to tephrosindicarboxylic acid (Part II, *loc. cit.*). Efforts in this direction, however, have been entirely unsuccessful; *e.g.*, the oxidation of the acetate of dehydrotoxicarol in acetone with aqueous potassium permanganate gave, in addition to 2-hydroxy-4 : 5-dimethoxybenzoic acid and rissic acid, a neutral product (an acetate), m. p. 149°, which did not appear to be suitable for further step-wise degradation. Consequently we turned our attention to the hydrolytic fission of dehydrotoxicarol and of dihydrotoxicarolic acid, having as our objective the isolation of phenols analogous to tubanol and dihydrotubanol.

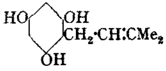
Degradation of dehydrotoxicarol with warm aqueous sodium hydroxide under a variety of conditions failed to give the expected product, but scission of dihydrotoxicarolic acid with hot 50% reagent yielded a crystalline dihydric phenol, $C_{11}H_{14}O_3$, which behaved as a saturated compound in the presence of hydrogen and a palladium–charcoal catalyst, formed a *diacetate* insoluble in cold aqueous sodium hydroxide, did not contain a carbonyl group, and appeared to have one ethereal oxygen atom. On the basis of the 2 : 2-dimethyl-Δ^3-chromen hypothesis and the fact that toxicarol has been shown to contain a phloroglucinol residue this substance was considered likely to be 5 : 7-*dihydroxy*-2 : 2-*dimethylchroman* (II); the properties of the phenol appeared to exclude a structure of the type (III) and from the arguments presented in Part V (*loc. cit.*) the dihydrofuran structure (IV) was considered improbable. That the compound has formula (II) is conclusively established by the fact that it was found to be identical with authentic 5 : 7-dihydroxy-2 : 2-dimethylchroman obtained in excellent yield by the application of Clemmensen's method of reduction to 5 : 7-*dihydroxy*-2 : 2-*dimethylchromanone* (VI, R = H).



(I.)



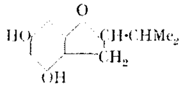
(II.)

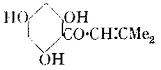


(III.)

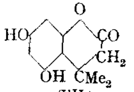
Although the condensation of phloroglucinol and ββ-dimethylacryl chloride with the aid of aluminium chloride gives a good yield of the chromanone (VI, R = H), the reaction does not afford conclusive evidence regarding the structure of the product and, since the standard chromanone synthesis (Robinson and co-workers, J., 1926, 945) is inapplicable,

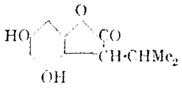
the structure of the compound has been deduced indirectly. It behaves as a saturated substance towards hydrogen in the presence of a palladium catalyst and forms a 2 : 4-*dinitrophenylhydrazone* and a *dimethyl ether* (VI, R = Me) which is insoluble in cold aqueous sodium hydroxide and does not give a ferric reaction, properties sufficing to distinguish the chromanone from the isomeric compounds (V), (VII), and (VIII) but not from the β-*coumaranone* (XII, R = H), all of which could conceivably have been formed by the Friedel–Crafts reaction. Although under certain conditions the chromanone is accompanied by small amounts of a by-product, no trace of an isomeric compound has been observed. The by-product, which has not yet been obtained analytically pure, appears to have the formula $C_{16}H_{18}O_5$, as it gives a *mono-2 : 4-dinitrophenylhydrazone* agreeing with this composition and is in all probability of the type (IX).

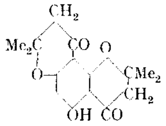

(IV.)

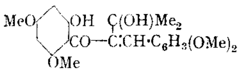

(V.)

(VI.)


(VII.)


(VIII.)

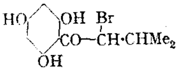

(IX.)

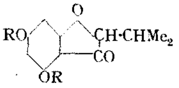

(X.)

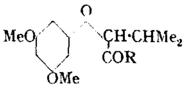
On general grounds it is almost certain that the formation of the chromanone (VI, R = H) would proceed by way of the unsaturated ketone (V), a mechanism which is strictly analogous to that obtaining in the synthesis of flavanones by the condensation of cinnamoyl chlorides with *m*-dihydroxyphenols. Nevertheless cyclisation of the ketone (V) could obviously have taken the alternative route with the formation of the coumaranone (XII, R = H) and hence it was essential that clear proof of the chromanone structure of the product should be obtained. For this purpose evidence of the presence of the group $CO{\cdot}CH_2$ in the dimethyl ether of the chromanone would have been conclusive, but our efforts to demonstrate this by standard methods were unsuccessful. Condensation of the dimethyl ether with veratraldehyde in alcoholic sodium hydroxide led to the formation of a compound, m.p. 152·5—153°, which, from appearance (yellow colour) and crimson-red coloration with concentrated sulphuric acid, appeared to be a benzylidene derivative of the chromanone, but which unexpectedly gave a dark red coloration with alcoholic ferric chloride. Analysis indicated the presence of a molecule of water more than that required for 5 : 7-dimethoxy-2 : 2-dimethyl-3-veratrylidenechromanone and hence it would seem that this compound is the styryl derivative (X). This is supported by the fact that when a solution of the chromanone dimethyl ether in 5% alcoholic potassium hydroxide is kept for 24 hours at room temperature the product obtained on acidification has the properties of an *o*-hydroxyphenyl ketone. On the other hand attempts to form a veratrylidene derivative by the standard hydrogen chloride–acetic acid method led to the isolation of an almost colourless, amorphous product which could not be purified and may have contained a bis-derivative of the aldehyde. Similarly, condensation of the dimethyl ether with 2-hydroxy-4-methoxybenzaldehyde in ethyl acetate by means of hydrogen chloride in the usual manner yielded a red chromenopyrylium-like product which has not yet been obtained pure. Efforts to prepare an *iso*nitroso-derivative of the dimethyl ether by the usual method were equally unsuccessful; a compound, m. p. 124—125°, was invariably obtained in small yield, which, however, did not contain nitrogen and was accompanied by a considerable amount of impurities giving a ferric reaction.

Since these attempts to obtain decisive evidence for the chromanone structure proposed for the Friedel–Crafts product (VI, R = H) and its dimethyl ether (VI, R = Me) were unpro-

ductive, the synthesis of the isomeric β-*coumaranone* (XII, R = H) was next investigated. In contrast to the formation of the chromanone (VI, R = H) the condensation of phloro-


(XI.)


(XII.)


(XIII.)

glucinol with α-bromo*iso*valeryl chloride in nitrobenzene by the Friedel–Crafts method furnished, along with traces of a bromo-compound, a small yield of a product which appeared to be (XII, R = H). This compound behaves as a saturated substance towards hydrogen in the presence of a palladium or platinum catalyst, but, unlike the isomeride (VI, R = H), does not appear to form a 2 : 4-dinitrophenylhydrazone readily and on reduction by Clemmensen's method gives, in addition to much amorphous material, only traces of a phenolic compound. By the methyl iodide–potassium carbonate method an alkali-insoluble methylation product was obtained which could not be satisfactorily purified from more highly methylated by-products (probably trimethyl ether of enolic form of coumaranone) but appeared to consist mainly of the dimethyl ether (XII, R = Me) since it gave rise to a good yield of a 2 : 4-*dinitrophenylhydrazone*, subsequently found to be identical with the 2 : 4-dinitrophenylhydrazone of authentic 4 : 6-dimethoxy-2-*iso*propyl-3-coumaranone (XII, R = Me). The latter compound was prepared by an unambiguous method and hence the β-coumaranone structure of (XII, R = H) is established. Further, since comparison of the 2 : 4-dinitrophenylhydrazones of the β-coumaranone (XII, R = Me) and of the chromanone dimethyl ether (VI, R = Me) showed that the two compounds were isomeric and not identical, therefore the chromanone structure assigned to the latter ether and the parent dihydroxy-compound (VI, R = H) is confirmed. The analogous formation of 7-hydroxy-2 : 2-dimethylchromanone and of 6-hydroxy-2-*iso*propyl-3-coumaranone from resorcinol and the appropriate acid chlorides has also been established (compare Arima and Okamoto, *J. Chem. Soc. Japan*, 1929, **50**, 344), thus affording collateral evidence for the structures herein assigned to the phloroglucinol derivatives. These results will be described in a subsequent communication.

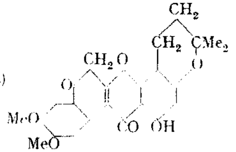
In view of the established formation of the chromanone (VI, R = H) when ββ-dimethylacryl chloride is employed in the Friedel–Crafts reaction the β-coumaranone (XII, R = H) must arise from the intermediate α-bromo-ketone (XI) by direct loss of hydrogen bromide without the formation of an unsaturated ketone (V). This cyclisation may well occur during the process of steam-distillation necessarily employed in working up the reaction mixture.

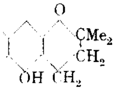
The authentic coumaranone (XII, R = Me) was prepared according to a standard procedure (Stephen and co-workers, J., 1936, 896): Interaction of the sodium derivative of phloroglucinol dimethyl ether and ethyl α-bromo*iso*valerate gave rise to a satisfactory yield of the ester (XIII, R = OEt), readily hydrolysed to the acid (XIII, R = OH). Cyclisation of the acid chloride (XIII, R = Cl) in benzene with aluminium chloride furnished a product from which the coumaranone (XII, R = Me) was obtained as a viscous oil, conveniently characterised by the formation of a 2 : 4-dinitrophenylhydrazone.

Although the chromanone structure of 5 : 7-dihydroxy-2 : 2-dimethylchromanone (VI, R = H) normally implies that the reduction product is the chroman (II), the ease of opening of the chromanone ring system (VI, R = Me) under certain conditions (see also experimental section) led us to consider the possibility that, on application of the Clemmensen reaction to (VI, R = H), reduction might be preceded by ring scission to give (V), resulting in the formation of (III), which could then undergo cyclisation to give the dihydrofuran (IV). The evidence at our disposal, however, appears to exclude this mechanism; *e.g.*, by analogy with unsubstituted chromanones and flavanones a ring system of the type (VI) would not be expected to open readily in the presence of acidic reagents; reduction of the chromanone appears to proceed normally, giving an excellent yield of (II) [compare β-coumaranone (XII, R = H)]. In any case, even if the reduction of the chromanone (VI, R = H) did take place by way of the intermediate (III), there is substantial evidence that compounds

of the latter type cyclise to chroman and not coumaran systems, *e.g.*, formation of β-dihydrorotenone and its relationship to deguelin and tephrosin (Part II, J., 1932, 1384; conversion of coumarins into chromanols and chromens, Heilbron and Hill, J., 1927, 2005). Attempts to obtain independent evidence on this question by oxidation of the chroman (II) have so far been unsuccessful.

(XIV.)





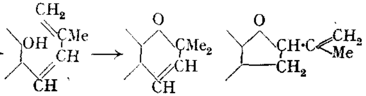
(XV.)

The isolation of the chroman (II) together with the structures established for *apo*- and dehydro*apo*-toxicarol in Part V (*loc. cit.*) affords substantial proof that dihydrotoxicarolic acid is represented by formula (I) and that dehydrodihydrotoxicarol has formula (XIV) or (XV). Further, since the ethylenic linkage of toxicarol is known to be present in the C_5 residue lost in the formation of *apo*toxicarol, it is now clear that toxicarol contains a 2 : 2-dimethyl-Δ^3-chromen residue and hence the alternative structures suggested for toxicarol, dehydrotoxicarol, and for dihydrotoxicarol in Part V are substantiated.

Formation of Acetone from 2 : 2-Dimethyl-Δ^3-chromens.—The formation of acetone by hydrolytic fission appears to be a general property of certain natural 2 : 2-dimethyl-Δ^3-chromens, deguelin, toxicarol, xanthoxyletin and xanthyletin (Part V, *loc. cit.*; J., 1936, 627, 1828) and in these cases this type of scission takes place much more readily than in the case of analogous compounds substituted in the 4-position; thus we have observed that the formation of acetone could not be detected when 7-hydroxy-2 : 2 : 4-trimethyl-Δ^3-chromen was boiled with 50% aqueous sodium hydroxide for 3 hours. Under the experimental conditions employed for the hydrolysis of the natural chromens (*loc. cit.*) it is extremely unlikely that the formation of acetone arises by fission across the double bond, *i.e.*, between the 3- and the 4-C atom of the chromen system, as a first step. This route would doubtless lead to the production of α-hydroxy*iso*butyric acid as an intermediate stage and, although this compound is stated to give acetone on fusion with solid sodium hydroxide, it is stable under conditions considerably more drastic than those necessary for the fission of the Δ^3-chromen systems of the aforementioned natural compounds.

In view of the occurrence of members of the rotenone series—rotenone, deguelin, tephrosin, and toxicarol—in the same or closely related plant species, and of the fact that these compounds contain the C_5 unit, ${}^{C}_{C}{>}C{-}C{-}C$, embodied either in a 2 : 2-dimethyl-Δ^3-chromen (type XVII) or in an isomeric coumaran system (type XVIII) it is reasonable to assume that both structures originate from a common type of intermediate, *e.g.* (XVI). On the further assumption that the attachment of the C_5 residue is one of the end processes in the phytochemical production of these compounds we may express the formation of the intermediate type (XVI) thus :

Me_2CO + $Me{\cdot}CHO$ ⟶ $Me_2C(OH){\cdot}CH_2{\cdot}CHO$ [or $CH_2{:}CMe{\cdot}CH_2{\cdot}CHO$] ⟶



(XVI.) (XVII.) (XVIII.)

The substance (XVI) could then undergo cyclisation in two ways, forming either the chromen (XVII) or the dihydrocoumarone (XVIII). Reversal of this scheme offers a feasible mechanism for the production of acetone by hydrolytic fission of 2 : 2-dimethyl-Δ^3-chromens, unsubstituted in the 3- and 4-positions, analogous to that suggested by Heilbron and Hill (*loc. cit.*) for the decomposition of 2 : 2-diphenyl-4-methyl-Δ^3-chromens, the final stage of

which represents the reversal of an aldol condensation. This mechanism, as indicated by these authors, finds a close analogy in the fission of certain coumarins discovered by Baker (J., 1925, **127**, 2349); *e.g.*, 7-hydroxy-3-phenyl-4-methylcoumarin gives mainly resorcinol and benzyl methyl ketone, which must arise by way of α-phenylacetoacetic acid.

EXPERIMENTAL.

Oxidation of Dehydrotoxicarol Acetate with Potassium Permanganate.—Treatment of dehydrotoxicarol (2·7 g.) with acetic anhydride (10 c.c.) and pyridine (5 c.c.) on the steam-bath for 2 hours gave the acetate, which formed pale straw-coloured needles or rods, m. p. 231—232°, identical with a specimen obtained by Clark's method (*J. Amer. Chem. Soc.*, 1931, **53**, 2264).

A solution of potassium permanganate (1·87 g.) in water (50 c.c.) was added to a well-stirred mixture of the acetate (1·7 g.) in acetone (750 c.c.) in the course of 1½ hours. Next day the manganese dioxide was recovered by filtration, the greater part of the acetone evaporated in a vacuum, the residual liquor treated with excess of aqueous sodium carbonate, and the insoluble product (A) collected. Acidification of the aqueous filtrate precipitated 2-hydroxy-4 : 5-dimethoxybenzoic acid, which had m. p. 213—214° after repeated crystallisation from aqueous acetone and was identical with a synthetical specimen (J., 1931, 2432). The precipitate of manganese dioxide was extracted with boiling water (20 c.c. × 5), and the combined extracts acidified with hydrochloric acid (Congo-red) and concentrated in a vacuum. After the removal of a small quantity of 2-hydroxy-4 : 5-dimethoxybenzoic acid, the residual liquor on extraction with ether gave a small amount of rissic acid, which formed colourless prisms, m. p. 256°, from methyl alcohol and was identified by comparison with an authentic specimen (J., 1932, 1380).

The aforementioned solid (A) was found to consist of a mixture of unchanged dehydrotoxicarol acetate and a neutral compound (B), from which the latter was extracted by means of warm methyl alcohol. Evaporation of the extracts left (B) as colourless plates contaminated with a small amount of dehydrotoxicarol acetate, which was removed by means of warm benzene (30—35°). Repeated crystallisation of the residue from dilute acetone and then dilute methyl alcohol gave (B) in colourless diamond-shaped plates, m. p. 149° after sintering at 143° (Found in air-dried material: C, 59·4, 59·8, 59·9; H, 5·5, 5·4, 5·5%. Found in a specimen dried in a vacuum at 110°: C, 60·6, 60·7, 60·8; H, 5·3, 5·2, 5·7; OMe, 14·4; CH_3·CO, 10·1%). This compound, which had a negative ferric reaction, was insoluble in aqueous sodium carbonate, but slowly dissolved in 8% aqueous sodium hydroxide. Acidification of the alkaline solution gave an amorphous solid having a green ferric reaction.

Hydrolytic Fission of Dihydrotoxicarolic Acid.—A mixture of the acid (Clark, *J. Amer. Chem. Soc.*, 1932, **54**, 2546) (5 g.) and 50% aqueous potassium hydroxide (20 c.c.) was heated (oil-bath) in nitrogen to 200—205° in the course of 14 minutes and then maintained at this temperature for 10 minutes. A solution of the cooled reaction mixture in water (150 c.c.) was acidified with hydrochloric acid (Congo-red), warmed to about 70°, mixed with charcoal, and filtered (wash charcoal with 70 c.c. of water). After the addition of excess of sodium bicarbonate the filtrate was thoroughly extracted with ether (40 c.c. × 10), and the combined extracts washed with brine, dried, and evaporated, leaving 5 : *7-dihydroxy-*2 : *2-dimethylchroman* as a light brown oil which gradually solidified. Crystallisation from benzene and then several times from water (charcoal) gave the compound in colourless hexagonal prisms (1 g.), m. p. 162—163°, readily soluble in ethyl or methyl alcohol, acetone, and ethyl acetate (Found: C, 68·1; H, 7·4. $C_{11}H_{14}O_3$ requires C, 68·0; H, 7·2%). In alcohol the ferric reaction is negative and in aqueous solution faint blue.

Acetylated with acetic anhydride (1·5 c.c.) and pyridine (0·5 c.c.) on the steam-bath for ½ hour, the chroman (0·5 g.) gave rise to the *diacetate*, which separated from a little methyl alcohol in colourless prisms, m. p. 86° (Found: C, 64·7; H, 6·7. $C_{15}H_{18}O_5$ requires C, 64·7; H, 6·5%). This derivative is soluble in the usual organic solvents and insoluble in cold aqueous sodium hydroxide.

ββ-Dimethylacrylic Acid.—Attempts to prepare this compound according to Dutt's method (*J. Indian Chem. Soc.*, 1924, **1**, 297) were unsuccessful.

A mixture of α-bromo*iso*valeric acid ("Organic Syntheses," XI, p. 20) (40 g.) and quinoline (80 g.) was heated to 140—150° and, when the vigorous reaction had ceased, then maintained at 165—170° for 20 minutes. After the addition of excess of dilute hydrochloric acid to the cooled reaction mixture ββ-dimethylacrylic acid was isolated with ether and purified by distillation in a vacuum; yield, 11·5 g. Crystallised from light petroleum (b. p. 40—60°), it had m. p. 67—68°.

When applied to α-bromo*iso*valeric acid, the method used by Perkin (J., 1896, **69**, 1470) for the preparation of acrylic acid from ethyl α-bromo*iso*valerate gave poor yields of an inferior product.

ββ-Dimethylacryl chloride (11 g.), b. p. 45—48°/12 mm., was prepared by gently warming the acid (12 g.) with thionyl chloride and purified by distillation in a vacuum.

5 : 7-Dihydroxy-2 : 2-dimethylchromanone (VI, R = H).—Aluminium chloride (15·2 g.) was dissolved in a mixture of nitrobenzene (200 c.c.) and phloroglucinol (16·2 g.) (agitate). ββ-Dimethylacryl chloride (11·5 g.) was then gradually introduced, and the reaction mixture kept at room temperature for 4 days. After the addition of ice (150 g.) and dilute hydrochloric acid (100 c.c.) the product, mixed with nitrobenzene, was isolated with ether, the nitrobenzene was removed by means of steam, and the hot aqueous liquor decanted from brown viscous resin. On being kept, the cooled aqueous solution slowly deposited the *chromanone*; a further quantity was obtained by extraction of the resinous residue with chloroform–light petroleum. Yield of crude material, 14·5 g. Recrystallised from chloroform or dilute alcohol, the compound formed colourless elongated prisms, m. p. 198°, readily soluble in alcohol, acetone or ethyl acetate and sparingly soluble in benzene (Found : C, 63·4; H, 5·7. $C_{11}H_{12}O_4$ requires 63·5; H, 5·8%). With alcoholic ferric chloride it gave a purple coloration.

Excess of 2 : 4-dinitrophenylhydrazine hydrochloride in dilute hydrochloric acid was added to a solution of the chromanone (0·7 g.) in alcohol (20 c.c.), and the mixture warmed for 10 minutes on the water-bath and then kept for 16 hours at room temperature. The resulting 2 : 4-*dinitrophenylhydrazone* formed blood-red needles, m. p. 277—278°, from alcohol (Found : N, 14·3. $C_{17}H_{16}O_7N_4$ requires N, 14·4%).

In the preparation of the chromanone it was found that the proportion of aluminium chloride employed had considerable effect upon the tractability of the product obtained and the foregoing procedure appeared to give an optimum result. In another experiment where phloroglucinol (1·25 mols.), acid chloride (1 mol.), and aluminium chloride (2·5 mols.) were allowed to interact in nitrobenzene for 7 days, the aqueous liquor left on removal of nitrobenzene gave only a small amount of the chromanone, and the resinous product, which did not yield crystalline material with solvents, was dissolved in ether and the solution extracted with aqueous sodium carbonate. In the course of the extraction a small amount of a solid sodium derivative crystallised. Decomposition of this material in a little methyl alcohol with acetic acid gave a compound (IX), which separated from light petroleum (b. p. 80—100°) in colourless elongated prisms, m. p. 134° (the melt becoming clear at 138°), giving a red coloration with alcoholic ferric chloride (Found in material dried at 90° : C, 66·9, 67·0; H, 6·3, 6·3; *M*, 245, 253. Calc. for $C_{16}H_{18}O_5$: C, 66·2; H, 6·2%; *M*, 290). The substance is soluble in alcohol, acetone, chloroform, benzene, or ethyl acetate and on treatment with 2 : 4-dinitrophenylhydrazine hydrochloride (method employed in the case of chromanone) gave rise to a 2 : 4-*dinitrophenylhydrazone*, which formed short red prisms, m. p. 267—268° (Found : C, 56·3; H, 4·9; N, 11·5. $C_{22}H_{22}O_8N_4$ requires C, 56·2; H, 4·7; N, 11·9%).

Acidification of the combined aqueous sodium carbonate extracts gave a further small amount of chromanone, m. p. 198° after purification.

5 : 7-Dimethoxy-2 : 2-dimethylchromanone (VI, R = Me).—Methylation of 5 : 7-dihydroxy-2 : 2-dimethylchromanone (2 g.) was effected with methyl iodide (4 c.c.) and potassium carbonate (7 g.) in boiling acetone (60 c.c.) in the course of about 7 hours; after 4 hours more iodide (2 c.c.) and more carbonate (3 g.) were added. When a test portion of the reaction mixture did not give a ferric reaction the potassium salts were removed by filtration (wash with excess acetone), the solvent evaporated, and an ethereal solution of the residue washed with dilute aqueous sodium hydroxide, dried, and evaporated. Crystallisation of the residual product from light petroleum (b. p. 60—80°) gave the *dimethyl ether* in colourless plates (1·7 g.), m. p. 104·5—105°, soluble in benzene or alcohol and having a negative ferric reaction [Found : C, 66·1; H, 6·9; OMe, 26·7. $C_{11}H_{10}O_2(OMe)_2$ requires C, 66·1; H, 6·8; OMe, 26·3%].

When a solution of the chromanone (0·4 g.) in alcohol (13 c.c.) was boiled with 2 : 4-dinitrophenylhydrazine hydrochloride (from 0·4 g. of the hydrazine) for 2 minutes, the 2 : 4-*dinitrophenylhydrazone* separated almost immediately; it formed blood-red needles (0·5 g.), m. p. 240°, from ethyl acetate (Found : N, 13·5. $C_{19}H_{20}O_7N_4$ requires N, 13·5%).

The product obtained by treating the chromanone with semicarbazide acetate in the usual manner separated from alcohol in colourless elongated prisms, m. p. 245° (Found : N, 13·7. Calc. for $C_{14}H_{19}O_4N_3$: N, 14·3%. Calc. for $C_{14}H_{19}O_4N_3,H_2O$: N, 14·0%). As this compound possesses the unexpected property of giving a reddish-brown coloration with alcoholic ferric chloride, it is probably the semicarbazone of a hydrated derivative of the chromanone, *i.e.*, of β : 2-dihydroxy-4 : 6-dimethoxy*iso*valerophenone (the semicarbazones of *o*-hydroxypropiophenone and of 3-chloro-2-hydroxyacetophenone give dark brownish-violet ferric reactions). On treatment with hot alcoholic 2 : 4-dinitrophenylhydrazine hydrochloride, however, this derivative was quan-

titatively converted into the 2 : 4-dinitrophenylhydrazone, m. p. 236—237°, which on being mixed with an authentic specimen, m. p. 240°, melted at 238—239°.

5 : 7-*Dihydroxy*-2 : 2-*dimethylchroman* (II).—A solution of 5 : 7-dihydroxy-2 : 2-dimethylchromanone (2 g.) in a mixture of alcohol (20 c.c.), acetic acid (10 c.c.), water (46 c.c.), and concentrated hydrochloric acid (34 c.c.) containing amalgamated zinc dust (Robinson and Shah, J., 1934, 1497) (80 g.) was kept at room temperature for 2 days, treated with 12% hydrochloric acid (20 c.c.), heated on the steam-bath for 1 hour, and then refluxed for 6 hours; more acid (20 c.c.) was added. The hot liquor was decanted, cooled, and extracted several times with ether and the combined extracts were well washed with aqueous sodium bicarbonate, dried, and evaporated, leaving the chroman, which separated from benzene and then water in colourless prisms (1·2 g.), m. p. 162—163°, identical in every way with the natural product (Found : C, 67·9; H, 7·3%). The diacetate formed colourless prisms, m. p. and mixed m. p. 86°, from a small volume of methyl alcohol.

4 : 6-*Dihydroxy*-2-iso*propyl*-3-*coumaranone* (XII, R = H).—α-Bromo*iso*valeryl chloride (18 g.) was slowly added to a cooled solution of phloroglucinol (14 g.) and aluminium chloride (15 g.) in nitrobenzene (200 c.c.), and the mixture kept for 4 days; more aluminium chloride (6 g.) was added after 2 days. The reaction mixture was very slowly heated to 60°, maintained at this temperature for 1 hour, cooled, and treated with excess of ice and hydrochloric acid. The mixture was extracted several times with ether, the combined extracts evaporated, and the nitrobenzene removed from the residue by a current of steam. On being kept, the residual aqueous liquor slowly deposited the *coumaranone* (4·5 g.), which formed colourless rhombic prisms, m. p. 196°, from dilute methyl alcohol, readily soluble in alcohol or ethyl acetate and sparingly soluble in benzene (Found : C, 63·3; H, 5·8. $C_{11}H_{12}O_4$ requires C, 63·5; H, 5·8%). Mixed with 5 : 7-dihydroxy-2 : 2-dimethylchromanone, this compound melted at 170—184°. With alcoholic ferric chloride it gave a purple coloration.

After the separation of the crude coumaranone the aqueous liquor deposited traces of a product containing bromine, m. p. 110—115° after being once recrystallised from water.

4 : 6-*Dimethoxy*-2-iso*propyl*(β)*coumaranone* (XII, R = Me).—(A) Ethyl α-bromo*iso*valerate (20 g.) was gradually added to a solution of phloroglucinol dimethyl ether (20 g.) in alcohol (80 c.c.) containing sodium ethoxide (from 3 g. of sodium) and next day the mixture was gently refluxed for 6 hours. After the removal of the greater part of the alcohol by distillation in a vacuum the residue was diluted with water, the solution extracted several times with ether, and the combined ethereal extracts washed with excess of 1% aqueous sodium hydroxide to remove unchanged phloroglucinol dimethyl ether, and evaporated. The residual mixed esters were hydrolysed with excess of 12% alcoholic sodium hydroxide at room temperature for 16 hours and on isolation in the usual manner the resulting 3 : 5-dimethoxy-α-phenoxy*iso*valeric acid (XIII, R = OH) (7 g.) (fraction, b. p. 160—170°/0·1 mm.) was separated from ββ-dimethylacrylic acid (6 g.) by distillation in a high vacuum and then crystallised from aqueous alcohol, forming colourless prisms, m. p. 92°.

Prepared by means of phosphorus pentachloride (4·4 g.), the acid chloride (from 5 g. of acid) was dissolved in purified benzene (50 c.c.) and then treated with aluminium chloride (2·9 g., added in the course of ½ hour). 3 Hours later, excess of ice and dilute hydrochloric acid was introduced, and the product and benzene isolated with ether. After having been washed with aqueous sodium bicarbonate to remove unchanged acid, the ether–benzene solution was evaporated, and the residue distilled in a high vacuum, giving a main fraction (2 g.). Redistillation of this material gave a clear, very viscous liquid, b. p. 140—150°/0·1 mm., which had the characteristic coumaranone odour and gave rise to a 2 : 4-*dinitrophenylhydrazone*, forming deep red needles, m. p. 185°, from alcohol (Found : N, 13·2. $C_{19}H_{20}O_7N_4$ requires N, 13·5%).

(B) 4 : 6-Dihydroxy-2-*iso*propylcoumaranone (1 g.) was methylated with methyl iodide (6 c.c., added in two portions) and excess of potassium carbonate in boiling acetone for 6 hours; a test sample did not give a ferric reaction. On isolation and removal of phenolic material by means of dilute sodium hydroxide the product was obtained as a viscous oil, which partly solidified and on treatment with hot alcoholic 2 : 4-dinitrophenylhydrazine hydrochloride gave rise to the coumaranone-2 : 4-dinitrophenylhydrazone, m. p. 185°, identical in every way with a specimen obtained by method (A) (Found : N, 13·4%).

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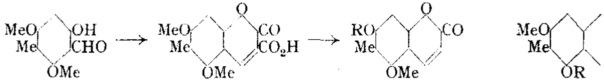
University of Liverpool. [*Received, December 18th*, 1936.]

58. *Constituents of* Zanthoxylum americanum (*Mill*). *Part III. The Constitution of Xanthoxyletin.*

By Alexander Robertson and T. S. Subramaniam.

In Part I (J., 1936, 627) it was clearly shown that *apo*xanthoxyletin was either 5-hydroxy-7-methoxy- or 7-hydroxy-5-methoxy-6-formylcoumarin and that the C_5 residue was present in a second heterocyclic system of the furan or (more probable) α-pyran type. The evidence described in the present memoir enables us to make a decision between each of these pairs of alternatives and consequently to develop complete structures for xanthoxyletin and its derivatives.

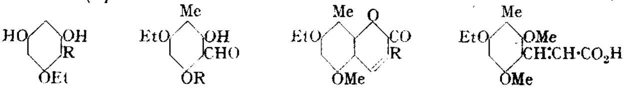
apo*Xanthoxyletin*.—Before proceeding to the orientation of this compound it was deemed advisable to confirm the structure of deoxy*apo*xanthoxyletin methyl ether (Part I, *loc. cit.*) by synthesis, a procedure now rendered possible by the recent preparation of *C*-methylphloroglucinol β-dimethyl ether (J., 1936, 1837). Accordingly, the *aldehyde* (I) was prepared from the latter ether in the usual manner and on condensation with cyanoacetic acid and subsequent hydrolysis of the product furnished the *coumarin-3-carboxylic acid* (II), which on decarboxylation gave rise to (III, R = Me), identical with the natural methyl ether of deoxy*apo*xanthoxyletin.



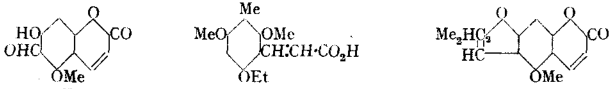
(I.) (II.) (III.) (IV.)

As it did not appear from the work of Curd and Robertson on derivatives of *C*-methylphloroglucinol (J., 1933, 437, 714) that a rational synthesis of the compounds having the structures possible for deoxy*apo*xanthoxyletin (type III, R = H, and IV, R = H) or for its *ethyl ether* was feasible, we decided to orient the latter ether by the following indirect method.

5-*Methoxy-7-ethoxy-8-methylcoumarin* (VII, R = H) was prepared from the *aldehyde* (VI, R = Me) by way of the *acid* (VII, R = CO_2H) and on hydrolysis and simultaneous methylation according to the general procedure (J., 1931, 1875) gave rise to 2 : 6-*dimethoxy-4-ethoxy-3-methylcinnamic acid* (VIII), identical with the cinnamic acid obtained from the isomeric deoxy*apo*xanthoxyletin ethyl ether by the same method. This result is possible only if the latter ether has the formula (III, R = Et), because a compound having the alternative structure (IV, R = Et) would give rise to 4 : 6-dimethoxy-2-ethoxy-3-methylcinnamic acid (X).



(V.) (VI.) (VII.) (VIII.)



(IX.) (X.) (XI.)

Accordingly, it follows, therefore, that deoxy*apo*xanthoxyletin is 7-hydroxy-5-methoxy-6-methylcoumarin (III, R = H) and hence *apo*xanthoxyletin is 7-hydroxy-5-methoxy-6-formylcoumarin (IX). Further, since it has been clearly shown that the C_5 unit is

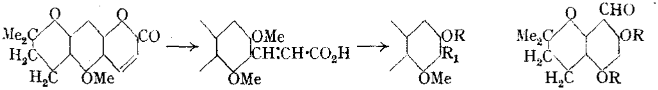
attached to the coumarin residue at the 6-position and to the oxygen atom appearing in the hydroxyl group in *apo*xanthoxyletin (Part I, *loc. cit.*), xanthoxyletin possesses the linear type of structure (XI).

The aldehyde (VI, R = Me) required for these experiments was conveniently prepared from phloroglucinol monoethyl ether by way of the stages (V, R = CHO), (V, R = Me), and (VI, R = H) and it may be noted that the successful production of (VI, R = Me) in this manner affords clear evidence that the orientations of the products formed by the application of the Gattermann reaction to phloroglucinol monoethyl ether and to (V, R = Me) and by the methylation of (VI, R = H) are identical with those of the analogous compounds obtained from the corresponding methyl ethers by the same methods respectively (Curd and Robertson, *loc. cit.*).

The 2 : 2-*Dimethyl*-Δ^3-*chromen Residue.*—The comparatively facile formation of acetone from xanthoxyletin by hydrolytic fission, in which respect there is a striking resemblance to toxicarol, led us to assume that xanthoxyletin contains a 2 : 2-dimethyl-Δ^3-chromen nucleus (compare Part I, *loc. cit.*), a view which is now completely vindicated.

Application of the Gattermann reaction to 5 : 7-dihydroxy-2 : 2-dimethylchroman gave rise to an *aldehyde* together with a compound which has not yet been fully investigated. Methylation of the former product yielded a dimethyl ether, which was characterised by the formation of a *semicarbazone* and a 2 : 4-*dinitrophenylhydrazone*. The same dimethyl ether of the formylchroman was obtained directly from specimens of 5 : 7-*dimethoxy*-2 : 2-*dimethylchroman* (XIV, R = Me; R_1 = H) prepared by the reduction of 5 : 7-dimethoxy-2 : 2-dimethylchroman-4-one and by the methylation of 5 : 7-dihydroxy-2 : 2-dimethylchroman.

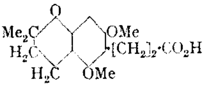
Ozonolysis of dihydroxanthoxyletin, which, as indicated in Part I (*loc. cit.*), we believed to contain a double bond in the α-pyrone ring, gave rise to a product (A) having the properties of an *o*-hydroxy-aldehyde and yielding a *monomethyl ether* which was characterised by the formation of a *semicarbazone* and a 2 : 4-*dinitrophenylhydrazone*. The same ether was also obtained by the oxidation of *O*-methyldihydroxanthoxyletinic acid with potassium permanganate or with ozone. Comparison of the semicarbazone and 2 : 4-dinitrophenylhydrazone of this ether with the respective derivatives of the dimethyl ether of the aldehyde obtained from 5 : 7-dihydroxy-2 : 2-dimethylchroman showed that the two compounds were isomeric and not identical, a result which we considered to be due to a difference in position of the formyl groups in the same chroman system rather than to the non-identity of the heterocyclic systems of the compounds.



(XII.) (XIII.) (XIV.) (XV.)

Oxidation of the monomethyl ether of (A) with aqueous potassium permanganate gave rise to an *acid* (B), which on decarboxylation yielded an oily product (C). That the latter product is identical with 5 : 7-dimethoxy-2 : 2-dimethylchroman (XIV, R = Me; R_1 = H) is clearly proved by the fact that by means of the Gattermann reaction it was converted into a compound shown to be identical with the aldehyde obtained from the authentic chroman dimethyl ether by comparison of their respective semicarbazones and 2 : 4-dinitrophenylhydrazones. Further, since it has already been shown that xanthoxyletin possesses a linear type of structure, the acid (B) has the structure (XIV, R = Me; R_1 = CO_2H) and therefore the aldehyde (A) and its methyl ether must be 7-*hydroxy*-5-*methoxy*- (XIV, R = H; R_1 = CHO) and 5 : 7-*dimethoxy*-6-*formyl*-2 : 2-*dimethylchroman* (XIV, R = Me; R_1 = CHO) respectively. Consequently the isomeride of the latter compound obtained from 5 : 7-dimethoxy-2 : 2-dimethylchroman is the 8-*formyl* derivative (XV, R = Me). In this connexion it is of interest to note that the orientation of the aldehyde (XV, R = H) prepared from the dihydroxychroman, which follows from the structure of its dimethyl ether (XV, R = Me), differs from that expected by analogy with the behaviour of *C*-

methylphloroglucinol β-monomethyl ether when submitted to the Gattermann reaction (Curd and Robertson, *loc. cit.*).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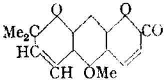
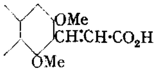

(XVII.)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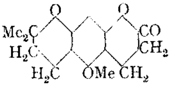
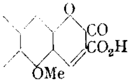
(XIX.)



(XX.)

From the foregoing results it follows that dihydroxanthoxyletin contains the 2 : 2-dimethylchroman residue and is represented by formula (XII) and consequently that *O*-methyldihydro- and *O*-methyltetrahydro-xanthoxyletinic acid have formulæ (XIII) and (XVI) respectively. Further, since it contains two double bonds, one of which is embodied in the C_5 residue and is preferentially attacked by hydrogen in the presence of a catalyst and by ozone, and the other, less reactive, in the α-pyrone ring, xanthoxyletin must be represented by the expression (XVII) and *O*-methylxanthoxyletinic acid by (XVIII). Finally, *tetrahydroxanthoxyletin*, which has now been obtained by catalytic reduction of dihydroxanthoxyletin in the presence of sodium hydroxide, followed by lactonisation of the resulting tetrahydro-acid, has the formula (XIX).

A partial synthesis of dihydroxanthoxyletin has been effected from the aldehyde (XIV, R = H; R_1 = CHO). Condensation of the latter compound with cyanoacetic acid and subsequent hydrolysis of the resulting salicylidenecyanoacetic acid gave rise to the *coumarin-3-carboxylic acid* (XX), which on decarboxylation yielded dihydroxanthoxyletin. Attempts to obtain xanthoxyletin by dehydrogenation of the latter compound have failed so far and the remaining step required to complete this synthesis, *viz.*, the conversion of the 5 : 7-dihydroxy-2 : 2-dimethylchroman into the aldehyde (XIV, R = H; R_1 = CHO), has not yet been effected.

In conclusion it may be noted that xanthyletin (*J.*, 1936, 1828) and xanthoxyletin constitute a new type of natural chromeno-α-pyrone analogous to the chromenodihydro-γ-pyrones, deguelin, tephrosin, and toxicarol (J., 1932, 1380; 1935, 681).

EXPERIMENTAL.

2-Hydroxy-4 : 6-dimethoxy-5-methylbenzaldehyde (I).—In the course of the synthesis of *C*-methylphloroglucinol β-dimethyl ether (J., 1936, 1837) required for this experiment the following modification of Pratt and Robinson's procedure (J., 1924, 125, 193) for the preparation of phloroglucinol dimethyl ether gave a satisfactory yield of phloroglucinol monomethyl ether; this method is superior to that starting from 3 : 5-dinitroanisole.

A solution of anhydrous phloroglucinol (50 g.) in methyl alcohol (200 c.c.) was saturated with dry hydrogen chloride in the course of 45 minutes; the rate of saturation was such that the alcohol did not boil. The mixture was then refluxed for 30 minutes, saturated again with hydrogen chloride at room temperature in the course of 45 minutes, kept for 12 hours, and evaporated in a vacuum. On isolation in the usual manner, followed by distillation in a vacuum, the product gave the monomethyl ether (25 g.) and the dimethyl ether (15 g.).

A solution of *C*-methylphloroglucinol β-dimethyl ether (1 g.) and hydrogen cyanide (1·5 c.c.) was saturated at room temperature with dry hydrogen chloride and next day the aldimine was collected, well washed with ether, and hydrolysed with water (30 c.c.) on the steam-bath for 15 minutes. The resulting *aldehyde* (0·65 g.) formed slender colourless needles, m. p. 85°, from dilute alcohol, giving a dark red coloration with alcoholic ferric chloride [Found : C, 61·2; H, 6·2; OMe, 31·4. $C_8H_6O_2(OMe)_2$ requires C, 61·2; H, 6·1; OMe, 31·6%].

5 : *7-Dimethoxy-6-methylcoumarin* (III, R = Me).—A mixture of the foregoing aldehyde (0·6 g.), cyanoacetic acid (5 c.c. of a solution prepared according to directions of Phelps and Tillotson, *Amer. J. Sci.*, 1908, 26, 267), and 20% aqueous sodium hydroxide (4 c.c.) was agitated

for 2 hours and 1 hour later the resulting solution was acidified (Congo-red) with dilute hydrochloric acid. The yellow micro-crystalline precipitate of 4 : 6-dimethoxy-5-methylsalicylidene-cyanoacetic acid (0·7 g.), m. p. 240—243° (decomp.), was collected, washed, and hydrolysed by being boiled with 4% hydrochloric acid for 40 minutes, yielding 5 : *7-dimethoxy-6-methylcoumarin-3-carboxylic acid* (II), which separated from the hot reaction mixture in pale yellow needles (0·6 g.), m. p. 233—234° after recrystallisation from dilute alcohol (Found : C, 59·1 ; H, 4·7. $C_{13}H_{12}O_6$ requires C, 59·1 ; H, 4·6%).

This acid (0·4 g.) was decarboxylated by being boiled with quinoline (40 c.c.) containing copper-bronze (3 g.) for 20 minutes and after addition of excess of dilute hydrochloric acid to the filtered reaction mixture the *coumarin* was isolated with ether and purified by sublimation in a high vacuum (colourless needles) and then by recrystallisation from benzene–light petroleum (b. p. 60—80°), forming slender colourless needles (0·2 g.), m. p. 135—136°, undepressed by admixture with a natural specimen [Found : C, 65·4 ; H, 5·5 ; OMe, 27·8. Calc. for $C_{10}H_6O_2(OMe)_2$: C, 65·5 ; H, 5·5 ; OMe, 28·2%].

Vigorous acetylation of the aldehyde (I) (1·25 g.) with sodium acetate (3 g.) and acetic anhydride (3 c.c.) at 155—160° for 7 hours gave rise to an inferior yield of the same coumarin (0·1 g.), m. p. 134—135° after sublimation and recrystallisation.

2 : *4-Dihydroxy-6-ethoxybenzaldehyde* (V, R = CHO).—Of a number of trial experiments the following gave the best yield of phloroglucinol monoethyl ether (compare Weidel and Pollak, *Monatsh.*, 1897, **18**, 355). Dry hydrogen chloride was led into a solution of phloroglucinol (60·0 g.) in alcohol (100 c.c.) for 45 minutes, at such a rate as to keep the temperature of the mixture at 60°. After being kept at room temperature for 18 hours, the reaction mixture was treated with water (20 c.c.) and then 8% aqueous sodium hydroxide (100 c.c.), and the product isolated with ether. By repeated distillation in a high vacuum this material was resolved into phloroglucinol monoethyl ether (20 g.), b. p. 157—160°/0·5 mm., and diethyl ether (20 g.), b. p. 143—145°/0·5 mm.

Condensation of the monoethyl ether (8 g.) and hydrogen cyanide (10 c.c.) in ether (80 c.c.) with excess of hydrogen chloride gave an aldimine which on hydrolysis with water (100 c.c.) on the steam-bath during ½ hour furnished the *aldehyde*, forming yellow needles (7 g.) from dilute alcohol (charcoal). After sublimation in a high vacuum, followed by recrystallisation from dilute alcohol, the crystals, m. p. 169·5°, retained a pale yellow colour [Found : C, 59·4 ; H, 5·5 ; OEt, 24·8. $C_7H_5O_3(OEt)$ requires C, 59·3 ; H, 5·5 ; OEt, 24·7%]. This compound is insoluble in cold water, benzene, or light petroleum and gives an intense red coloration with aqueous or alcoholic ferric chloride. The 2 : *4-dinitrophenylhydrazone*, which is almost insoluble in hot alcohol, separated from warm ethyl acetate in small, dark red prisms, m. p. 263—264° (Found : N, 15·3. $C_{15}H_{14}O_7N_4$ requires N, 15·5%).

Reduction of this aldehyde (3 g.), dissolved in acetic acid (100 c.c.), was readily effected with hydrogen (approx. 2 mols. absorbed) and a palladium–charcoal catalyst (prepared from 1 g. of charcoal and 20 c.c. of 1% palladium chloride solution) in about ½ hour. After removal of the catalyst the acetic acid was neutralised with aqueous sodium bicarbonate, and *C-methylphloroglucinol* β*-monoethyl ether* (V, R = Me) isolated with ether and purified by sublimation in a vacuum (about 140°/0·05 mm.) and then by crystallisation from chloroform, forming colourless slender prisms (2 g.), m. p. 130° after sintering at 128°, sparingly soluble in warm light petroleum or cold water and moderately soluble in warm benzene [Found : C, 64·5 ; H, 7·1 ; OEt, 26·8. $C_7H_7O_2(OEt)$ requires C, 64·3 ; H, 7·1 ; OEt, 26·8%]. The ferric reaction is pale blue in water and pale brown in alcohol.

2 : *6-Dihydroxy-4-ethoxy-3-methylbenzaldehyde* (VI, R = H).—Application of the Gattermann reaction to the aforementioned phenol (1·8 g.) in ether (50 c.c.) gave rise to the aldimine, which on hydrolysis with water (100 c.c.) on the steam-bath for ½ hour yielded the *aldehyde* in pale yellow needles (1·5 g.), m. p. 196—197° after purification from 75% alcohol (Found : C, 61·3 ; H, 6·2. $C_{10}H_{12}O_4$ requires C, 61·2 ; H, 6·1%). With alcoholic ferric chloride this compound gave a dark red coloration. The 2 : *4-dinitrophenylhydrazone* separated from ethyl acetate in deep orange, slender needles, m. p. 260—261° (Found : N, 14·7. $C_{16}H_{16}O_7N_4$ requires N, 14·9%).

Methylation of this aldehyde (1 g.) in boiling acetone (30 c.c.) with methyl iodide and potassium carbonate was complete in about ½ hour and gave rise to 2-hydroxy-6-methoxy-4-ethoxy 3-methylbenzaldehyde (VI, R = Me), which formed almost colourless needles, m. p. 130° after sintering at 128°, from alcohol [Found : C, 63·0 ; H, 6·7 ; AlkylO, 15·2. Calc. for $C_8H_6O_2(OMe)(OEt)$: C, 62·9 ; H, 6·7 ; AlkylO, 15·2%]. This material was identical with a specimen, m. p. 130° after sintering at 128°, prepared according to Curd and Robertson (J., 1933, 719), who give m. p. 126—127°. In this connexion it may be noted that 2 : 4-dihydroxy-6-methoxy-3-methyl-

benzaldehyde, which Curd and Robertson (*loc. cit.*) describe as forming golden-yellow needles from alcohol, has again been found to retain this colour when purified by crystallisation only, but on sublimation in a high vacuum, followed by recrystallisation, formed pale yellow, almost colourless needles, m. p. 239—240°.

Catalytic reduction (approx. 2 mols. of hydrogen absorbed) of 2 : 6-dihydroxy-4-ethoxy-3-methylbenzaldehyde (1 g.), dissolved in acetic acid (100 c.c.) containing charcoal and palladium chloride (20 c.c. of a 10% solution), gave rise to 2 : 4-dihydroxy-6-ethoxy-*m*-xylene, m. p. 130—131°, having a pale blue ferric reaction (Herzig and Hauser, *Monatsh.*, 1900, **21**, 869) [Found : C, 65·7; H, 7·6; OEt, 24·7. Calc. for $C_8H_9O_2(OEt)$: C, 65·9; H, 7·7; OEt, 24·7%].

5-Methoxy-7-ethoxy-8-methylcoumarin-3-carboxylic Acid (VII, R = CO_2H).—Acidification of the reaction mixture obtained by the interaction of 2-hydroxy-6-methoxy-4-ethoxy-3-methylbenzaldehyde and cyanoacetic acid (5 c.c. of Phelps and Tillotson's solution, *loc. cit.*) in 20% aqueous sodium hydroxide (6 c.c.) during 5 hours (agitate) gave rise to a salicylidenecyanoacetic acid, which on hydrolysis with boiling 4% hydrochloric acid for 1 hour yielded the *coumarin-3-carboxylic acid*. This compound, which was insoluble in benzene or alcohol, separated from acetone in slender needles, m. p. 238—239° after sintering at 230°, which decomposed at 250° (Found : C, 60·3; H, 5·0. $C_{14}H_{14}O_6$ requires C, 60·43; H, 5·1%).

5-Methoxy-7-ethoxy-8-methylcoumarin (VII, R = H).—The foregoing acid (0·5 g.) was boiled with quinoline (15 c.c.) containing copper-bronze (2 g.) for 5 minutes, and, after the addition of chloroform (500 c.c.), the filtered solution was washed with dilute hydrochloric acid to remove the quinoline, and then with aqueous sodium bicarbonate to remove traces of acid material. Evaporation of the solution left the *coumarin*, which formed slender colourless needles (0·3 g.), m. p. 167°, from alcohol, insoluble in hot benzene or light petroleum [Found : C, 66·7; H, 5·8; AlkylO, 14·3. $C_{10}H_6O_2(OMe)(OEt)$ requires C, 66·7; H, 6·0; AlkylO, 13·7%].

Fission of this coumarin (0·8 g.), followed by methylation of the resulting *o*-hydroxycinnamic acid with 20% aqueous sodium hydroxide and methyl sulphate according to Canter and Robertson's method (*loc. cit.*), gave the methyl ester of 2 : *6-dimethoxy-4-ethoxy-3-methylcinnamic acid* (VIII), which formed colourless needles, m. p. 78°, from light petroleum (b. p. 40—60°). Hydrolysis of this ester with boiling 7% alcoholic potassium hydroxide for 15 minutes yielded the acid, which formed small colourless prisms (0·7 g.) from benzene, m. p. 164—165° [Found : C, 63·3; H, 6·8; AlkylO, 18·3. $C_{10}H_7O_2(OMe)_2(OEt)$ requires C, 63·2; H, 6·8; AlkylO, 18·0%].

*Deoxy*apo*xanthoxyletin Ethyl Ether* (III, R = Et).—Ethylation of deoxy*apo*xanthoxyletin (0·5 g.) in boiling acetone (30 c.c.) with ethyl iodide (two portions of 3 c.c.) and potassium carbonate (5 g.) during 1¾ hours gave rise to the *ethyl ether* as an oil, which solidified on trituration with water and then separated from alcohol in colourless needles (0·4 g.), m. p. 135°, insoluble in benzene or light petroleum [Found : C, 66·6; H, 6·1; AlkylO, 13·3. $C_{10}H_6O_2(OMe)(OEt)$ requires C, 66·7; H, 6·0; AlkylO, 13·7%]. Ethereal and alcoholic solutions of this coumarin exhibit a blue fluorescence.

By the usual procedure of hydrolysis and methylation this compound was converted almost quantitatively into *methyl* 2 : *6-dimethoxy-4-ethoxy-3-methylcinnamate*, which formed clusters of needles, m. p. 78·5°, from light petroleum (b. p. 40—60°), identical with a synthetical specimen obtained from 5-methoxy-7-ethoxy-8-methylcoumarin (Found : C, 64·3; H, 7·1. $C_{15}H_{20}O_5$ requires C, 64·3; H, 7·1%).

Hydrolysis of the ester gave rise to the cinnamic acid (VIII), which was purified by means of aqueous sodium bicarbonate and then by crystallisation from benzene–light petroleum (b. p. 60—80°), forming small colourless prisms, m. p. 165°, undepressed by admixture with a synthetical specimen (Found : C, 63·2; H, 6·8; AlkylO, 17·7%).

5 : *7-Dihydroxy-8-formyl-2* : *2-dimethylchroman* (XV, R = H).—The reaction mixture, obtained by saturating a solution of 5 : 7-dihydroxy-2 : 2-dimethylchroman (Robertson and co-workers, this vol., p. 285) (1 g.) in ether (50 c.c.) containing hydrogen cyanide (2 c.c.) with hydrogen chloride, was kept for one day and mixed with more ether (30 c.c.), and the ethereal solution decanted from the solid (wash with ether). A solution of the product in water (30 c.c.) was hydrolysed on the water-bath for 10 minutes; after cooling, the aqueous liquor was decanted from the oily material which had separated, and the residue triturated with water until it solidified. The dried solid was extracted several times with a boiling mixture of chloroform and light petroleum (b. p. 60—80°); on cooling, the extracts deposited a product in needles, which on recrystallisation from alcohol had m. p. 123—124° and gave a dark red ferric reaction in alcohol. The products obtained by treating this material with semicarbazide acetate and with 2 : 4-dinitrophenylhydrazine hydrochloride could not be purified.

After being heated on the steam-bath for 10 minutes, the combined aqueous liquor and

aqueous washings from the foregoing crude product slowly deposited the 8-*formylchroman*, which formed colourless needles (0·1 g.), m. p. 179—180°, from dilute alcohol (Found : C, 65·1 ; H, 6·4. $C_{12}H_{14}O_4$ requires C, 64·9 ; H, 6·3%). This compound gives with alcoholic ferric chloride a deep purple-red coloration which becomes bluish-red on the addition of much alcohol and wine-red on dilution with water.

The use of zinc chloride in the Gattermann reaction gave rise to a resinous product from which only the substance, m. p. 123—124°, could be isolated.

5 :7 -*Dimethoxy*-2 : 2-*dimethylchroman* (XIV, R = Me ; R_1 = H).—A mixture of 5 : 7-dimethoxy-2 : 2-dimethylchromanone (Robertson and co-workers, *loc. cit.*) (1 g.), amalgamated zinc dust (20 g.), acetic acid (10 c.c.), and 12% hydrochloric acid (50 c.c.) was refluxed for 5 hours ; after 3 hours more hydrochloric acid (50 c.c.) was added. The cooled acid liquors were extracted several times with ether, and the combined ethereal extracts washed with dilute aqueous sodium hydroxide and then with water, dried, and evaporated. Distillation of the residual oil in a high vacuum gave the *chroman* as an almost colourless oil (0·5 g.), b. p. 105°/0·05 mm. (Found : C, 70·4 ; H, 8·2. $C_{13}H_{18}O_3$ requires C, 70·3 ; H, 8·1%). The same compound, b. p. 105—106°/0·05 mm., was obtained by methylation of 5 : 7-dihydroxy-2 : 2-dimethylchroman (1 g.) in acetone (30 c.c.) with excess of methyl iodide and potassium carbonate during 3 hours (Found : C, 70·5 ; H, 8·3%).

5 : 7-*Dimethoxy*-8-*formyl*-2 : 2-*dimethylchroman* (XV, R = Me).—(A) Methylation of 5 : 7-dihydroxy-8-formyl-2 : 2-dimethylchroman, m. p. 179—180°, (0·4 g.) in acetone (30 c.c.) with methyl iodide and potassium carbonate during 3 hours gave the crude dimethyl ether, having a negative ferric reaction. An ethereal solution of this material was washed twice with aqueous sodium hydroxide, dried, and evaporated. Part of the resulting product was converted into the *semicarbazone*, which separated from hot alcohol in colourless needles, m. p. 217—218° (Found : C, 58·8 ; H, 6·7 ; N, 13·5. $C_{15}H_{21}O_4N_3$ requires C, 58·7 ; H, 6·8 ; N, 13·7%).

On addition of one drop of concentrated sulphuric acid to a solution of the remaining portion of the crude aldehyde and 2 : 4-dinitrophenylhydrazine (0·1 g.) in hot alcohol (5 c.c.) the 2 : 4-*dinitrophenylhydrazone* quickly separated in slender, dark red needles, m. p. 242—243° after recrystallisation from warm benzene (Found : C, 56·0 ; H, 5·2 ; N, 12·9. $C_{20}H_{22}O_7N_4$ requires C, 55·8 ; H, 5·1 ; N, 13·0%).

(B) The crystalline aldimine, obtained by saturating a solution of 5 : 7-dimethoxy-2 : 2-dimethylchroman (0·5 g.) in dry ether (30 c.c.), containing hydrogen cyanide (1 c.c.), with hydrogen chloride, was washed with ether and hydrolysed with water (30 c.c.) on the steam-bath for 20 minutes. The resulting aldehyde gave an almost quantitative yield of the semicarbazone, which separated from alcohol in needles, m. p. and mixed m. p. 217—218°.

Ozonolysis of Dihydroxanthoxyletin.—A stream of ozone and oxygen (rate of 40 c.c. per minute) was led into a solution of the dihydro-compound (1 g.) in chloroform (100 c.c.) for 2 hours, the solvent was evaporated in a vacuum, and the residue hydrolysed with water (50 c.c.) at room temperature for 16 hours and then on the steam-bath for 10 minutes. An ethereal solution of the product was extracted eight times with 8% aqueous sodium hydroxide (4 c.c.) and the combined extracts were diluted with twice their volume of water, treated with a little charcoal, filtered, and saturated with carbon dioxide. The precipitated 7-*hydroxy*-5-*methoxy*-6-*formyl*-2 : 2-*dimethylchroman* (XIV, R = H ; R_1 = CHO) was collected and purified by distillation in a high vacuum and then by crystallisation from dilute alcohol, forming colourless flat prisms, m. p. 85—86°, which were readily soluble in alcohol, light petroleum, or benzene, gave a dark claret coloration with alcoholic ferric chloride, reduced ammoniacal silver nitrate, and formed a red 2 : 4-dinitrophenylhydrazone [Found : C, 65·9 ; H, 6·8 ; OMe, 13·0. $C_{12}H_{13}O_3(OMe)$ requires C, 66·1 ; H, 6·8 ; OMe, 13·1%].

5 : 7-*Dimethoxy*-6-*formyl*-2 : 2-*dimethylchroman* (XIV, R = Me ; R_1 = CHO).—(A) Methylation of the foregoing aldehyde (0·6 g.) in boiling acetone (25 c.c.) with methyl iodide and potassium carbonate was complete after 2 hours (indicated by the disappearance of the yellow colour of the reaction mixture) and yielded 5 : 7-*dimethoxy*-6-*formyl*-2 : 2-*dimethylchroman*, which, after having been distilled in a high vacuum, separated from light petroleum in colourless prisms, m. p. 81—82° [Found : C, 67·0 ; H, 7·2 ; OMe, 25·2. $C_{12}H_{12}O_2(OMe)_2$ requires C, 67·2 ; H, 7·2 ; OMe, 24·8%]. The semicarbazone formed slender needles, m. p. 215—216°, from alcohol.

(B) A solution of *O*-methyldihydroxanthoxyletinic acid (Part I, *loc. cit.*) (2 g.) in acetone (80 c.c.), maintained at 50°, was treated with 1·4% aqueous potassium permanganate (200 c.c.) in the course of 2 hours. After having been cleared with sulphur dioxide, the reaction mixture was heated on the steam-bath with 8% sulphuric acid (10 c.c.) for 10 minutes and then extracted eight times with ether and the combined extracts were washed with aqueous sodium bicarbonate to remove acidic material, dried, and evaporated, leaving a residue which had the properties of

the aldehyde prepared by method (A) and was converted into the *semicarbazone*. This derivative separated from alcohol in slender needles (0·4 g.), m. p. 215·5—216·5°, identical with a specimen prepared by method (A) (Found: C, 58·4; H, 7·1; N, 12·8. $C_{15}H_{21}O_4N_3$ requires C, 58·6; H, 6·8; N, 13·7%).

A hot solution of 2 : 4-dinitrophenylhydrazine hydrochloride (0·13 g.) in alcohol (5 c.c.) containing 2 drops of concentrated sulphuric acid was added to a solution of the semicarbazone (0·2 g.) in the same solvent (10 c.c.), and the mixture boiled for 1 minute. The reaction mixture quickly became dark red and the *2 : 4-dinitrophenylhydrazone* separated in dark red needles. Recrystallised from ethyl acetate–alcohol, it formed rectangular prisms, m. p. 215—216° (Found: C, 56·0; H, 5·2; N, 12·7. $C_{20}H_{22}O_7N_4$ requires C, 55·8; H, 5·1; N, 13·0%).

(C) A stream of ozone and oxygen (rate of approx. 50 c.c. per minute) was led into a solution of O-methyldihydroxanthoxyletinic acid (2 g.) at 0° for 2 hours. After the removal of the solvent in a vacuum the product was hydrolysed with water (50 c.c.) at room temperature for 12 hours and then on the water-bath for 10 minutes; the resulting aldehyde was isolated with ether and converted into the semicarbazone, m. p. and mixed m. p. 215—216°, after purification from alcohol.

5 : 7-Dimethoxy-2 : 2-dimethylchroman-6-carboxylic Acid (XIV, R = Me; $R_1 = CO_2H$).—Oxidation of the foregoing aldehyde (1 g.), dissolved in acetone (20 c.c.), was effected at 60° with 3% aqueous potassium permanganate (50 c.c., added in the course of 1 hour). Next day the mixture was cleared with sulphur dioxide, and the *acid* (0·5 g.) precipitated with excess of dilute sulphuric acid and purified by crystallisation from dilute alcohol and then from dilute acetone, forming colourless needles, m. p. 142—143° (decomp.); a further quantity of the compound (0·2 g.) was isolated from the aqueous liquor with ether and separated from a little unchanged aldehyde by means of aqueous sodium bicarbonate [Found: C, 63·2; H, 7·1; OMe, 22·9. $C_{12}H_{12}O_3(OMe)_2$ requires C, 63·2; H, 6·8; OMe, 23·3%].

Decarboxylation of this acid (1 g.) at 144—145° in the course of 5 minutes yielded 5 : 7-dimethoxy-2 : 2-dimethylchroman (0·7 g.), which was purified by distillation in a high vacuum, b. p. 105°/0·05 mm. (Found: C, 70·4; H, 8·3%). On being submitted to the Gattermann reaction this material gave a rise to a good yield of 5 : 7-dimethoxy-8-formyl-2 : 2-dimethylchroman, which was characterised by conversion into the semicarbazone, m. p. 217—218°, identical with a specimen prepared from the authentic aldehyde (Found: C, 58·6; H, 6·7; N, 13·7; OMe, 21·0%). Similarly, the 2 : 4-dinitrophenylhydrazone had m. p. and mixed m. p. 243—244° (Found: C, 56·0; H, 5·1; N, 12·9%).

Tetrahydroxanthoxyletin (XIX).—A mixture of dihydroxanthoxyletin (Part I, *loc. cit.*) (1 g.) and hot alcohol (20 c.c.), containing 20% aqueous sodium hydroxide (2 c.c.), was agitated until a clear solution was obtained and a test sample did not give a precipitate or opalescence on addition of water. After dilution with water (50 c.c.) the disodium derivative of dihydroxanthoxyletinic acid was hydrogenated with hydrogen (absorption, approx. theoretical) and an active palladium–charcoal catalyst (from 0·2 g. of palladium chloride and 1 g. of charcoal), the catalyst removed by filtration, and the solution acidified (Congo-red) with 8% hydrochloric acid. On being heated in a vacuum at 180°/0·1 mm., the crystalline precipitate of tetrahydroxanthoxyletinic acid, needles, m. p. 150° (efferv.), which readily dissolved in aqueous sodium bicarbonate, was cyclised and the resulting *tetrahydroxanthoxyletin* simultaneously sublimed, forming colourless slender prisms. This compound separated from warm alcohol in tiny rhombic prisms, m. p. 121°, soluble in cold benzene and sparingly soluble in hot light petroleum (Found: C, 68·7; H, 6·8. $C_{15}H_{18}O_4$ requires C, 68·7; H, 6·9%). Mixed with dihydroxanthoxyletin, it melted at 115—117°.

Dihydroxanthoxyletin-3-carboxylic Acid (XX).—A mixture of 7-hydroxy-5-methoxy-6-formyl-2 : 2-dimethylchroman (1 g.), cyanoacetic acid (4 c.c. of a solution prepared by the method of Phelps and Tillotson, *loc. cit.*), and 20% aqueous sodium hydroxide (5 c.c.) was kept for 12 hours, diluted with water (20 c.c.), and acidified (Congo-red) with 8% hydrochloric acid. The precipitate was washed with water and boiled with 4% hydrochloric acid for 1½ hours. Recrystallisation of the resulting *coumarin-3-carboxylic acid* from alcohol gave elongated slender prisms (1·2 g.), m. p. 139—140°, readily soluble in aqueous sodium bicarbonate and giving a negative ferric reaction (Found: C, 63·1; H, 5·3. $C_{16}H_{16}O_6$ requires C, 63·2; H, 5·3%).

An intimate mixture of the acid (0·5 g.) and Kahlbaum's "Natur Kupfer" (0·5 g.) was heated at 190—195° for ½ hour; the resulting dihydroxanthoxyletin (XII), isolated from the reaction mixture by sublimation in a high vacuum, formed small, thick, rhombic prisms (0·3 g.). Purified from alcohol, it had m. p. and mixed m. p. 143° and was identical in every way with a natural specimen.

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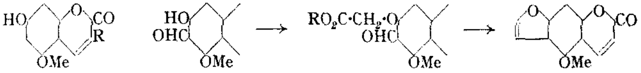
59. *Furano-compounds. Part I. A Synthesis of Bergapten.*

By WILLIAM N. HOWELL and ALEXANDER ROBERTSON.

THE accepted structure of bergapten, which depends on the analytical evidence of Thoms and Baetcke (*Ber.*, 1912, **45**, 3705), has now been confirmed by a synthesis of the compound from *apo*xanthoxyletin, the orientation of which has been established (preceding paper).



(I.) (II.) (III.) (IV.)

Interaction of (II) and ethyl bromoacetate in boiling acetone containing potassium carbonate gave an unexpectedly poor yield of the *ethyl* ester (III, R = Et), which was not improved by varying the relative amounts of the reactants. On hydrolysis this ester furnished the *acid* (III, R = H), which on cyclisation and simultaneous decarboxylation by means of boiling acetic anhydride containing sodium acetate yielded the furanocoumarin (IV), identical in every respect with natural bergapten.

The parent *coumarin* (I, R = H) has been obtained by decarboxylation of the *acid* (I, R = CO_2H), which was prepared by the cyanoacetic acid method, but the conversion of (I, R = H) into (II), the remaining step required to complete the synthesis of bergapten, has not yet been achieved.

EXPERIMENTAL.

7-Hydroxy-5-methoxycoumarin.—Interaction of 2 : 4-dihydroxy-6-methoxybenzaldehyde (2 g.) with cyanoacetic acid (12 c.c. of Phelps and Tillotson's solution; *Amer. J. Sci.*, 1908, **26**, 267) in 20% aqueous sodium hydroxide (12 c.c.) during 16 hours yielded 4-hydroxy-6-methoxysalicylidenecyanoacetic acid, which on hydrolysis with boiling 4% hydrochloric acid (200 c.c.) for ½ hour gave *7-hydroxy-5-methoxycoumarin-3-carboxylic acid* (1·8 g.); this formed needles, m. p. 264°, from 90% alcohol, insoluble in water (Found : C, 55·9; H, 3·3. $C_{11}H_8O_6$ requires C, 55·9; H, 3·4%). A solution of the acid in alcohol exhibited a blue fluorescence.

A mixture of the acid (1 g.) and quinoline (15 c.c.) containing copper-bronze (1 g.) was gently refluxed for ½ hour, cooled, filtered, and mixed with chloroform (600 c.c.). After the removal of the quinoline by means of dilute hydrochloric acid the chloroform solution was washed with aqueous sodium bicarbonate and dried. The *coumarin*, isolated from the product left on evaporation of the solvent by sublimation in a high vacuum, crystallised from 50% alcohol in slender needles, m. p. 246°, easily soluble in alcohol and sparingly soluble in chloroform or ether (Found : C, 62·9; H, 4·2. $C_{10}H_8O_4$ requires C, 62·5; H, 4·2%). An alcoholic solution of the compound does not fluoresce and does not give a ferric reaction.

7-Hydroxy-5-methoxy-6-formylcoumarin-7-O-acetic Acid (III, R = H).—The yield of *apo*xanthoxyletin obtained by ozonolysis of xanthoxyletin (*loc. cit.*) was improved by passing the stream of ozone and oxygen through the chloroform solution until the yellow colour was discharged; yield, 0·4 g. from 1 g. of xanthoxyletin.

A solution of *apo*xanthoxyletin (1 g.) and ethyl bromoacetate (1 g.; 1·3 mols.) in acetone (150 c.c.), containing excess of potassium carbonate, was refluxed for 18 hours and after the addition of more acetone (100 c.c.) the warm solution was filtered (wash potassium salts with acetone) and evaporated, leaving the *ester* (III, R = Et), which separated from alcohol in slender needles (0·2 g.), m. p. 136°, sparingly soluble in light petroleum and having a negative ferric reaction (Found : C, 58·9; H, 4·7. $C_{15}H_{14}O_7$ requires C, 58·8; H, 4·6%).

Acidification of an aqueous solution of the yellow potassium salts with hydrochloric acid gave unchanged *apo*xanthoxyletin (0·4 g.).

Hydrolysis of the ester (0·3 g.) with boiling 5% methyl-alcoholic potassium hydroxide (7 c.c.) for ½ hour gave rise to the *acid* (III, R = H), which separated from a small volume of acetone in tiny clusters of colourless needles (0·24 g.), m. p. 242° (decomp.), sparingly soluble in water, benzene, or carbon tetrachloride (Found : C, 56·4; H, 3·9. $C_{13}H_{10}O_7$ requires C, 56·1; H, 3·6%).

Bergapten (IV).—A mixture of the foregoing acid (0·3 g.), sodium acetate (1·5 g.), and acetic anhydride (15 c.c.) was refluxed for ½ hour, and, after decomposition of the anhydride with water, the mixture was neutralised with sodium bicarbonate and repeatedly extracted with ether.

Evaporation of the combined, dried extracts left bergapten, which was purified by recrystallisation from methyl alcohol, then aqueous alcohol, and finally benzene–light petroleum (b. p. 60—80°) with or without previous sublimation in a high vacuum and obtained in slender prisms, m. p. 188—189°, identical in every way with a natural specimen, m. p. 189° (Found: C, 66·7; H, 3·7. Calc. for $C_{12}H_8O_4$: C, 66·7; H, 3·7%).

A natural specimen was isolated from a fraction of bergamot oil rich in bergapten which was kindly presented to us by Messrs. Bush & Co., of London. This fraction was mixed with excess of light petroleum (b. p. 40—60°) and 48 hours later the precipitate was collected and repeatedly crystallised from methyl alcohol and then ethyl alcohol. The resulting bergapten had m. p. 189°.

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60. *Dichlorine Hexoxide.*

By CHARLES F. GOODEVE and FREDERICK D. RICHARDSON.

ALTHOUGH dichlorine hexoxide (Cl_2O_6) and chlorine trioxide (ClO_3) have been postulated as intermediates in a number of reactions involving the oxides of chlorine, little has been recorded of their physical and chemical properties.

It appears that the hexoxide was first obtained by Millon (*Annalen*, 1843, **46**, 311) by the action of sunlight on chlorine dioxide (ClO_2) cooled to below 20°. The oxide, which formed on the walls of the preparation vessel as a red liquid, decomposed even in the dark, but did not explode on heating. Eighty years later it was again prepared similarly (Bowen, J., 1923, **123**, 2328), and then Booth and Bowen (J., 1925, **127**, 510) found that on continued illumination the red oily liquid was converted into colourless dichlorine heptoxide. They showed that the liquid did not consist of the dioxide dissolved in anhydrous perchloric acid, and that its existence could not be explained on the basis of the then recognised oxides, *viz.*, Cl_2O, ClO_2, and Cl_2O_7. By analysis of the red liquid, Bodenstein, Harteck, and Padelt (*Z. anorg. Chem.*, 1925, **147**, 233) showed the oxygen : chlorine ratio to be 3 : 1; they also showed, by depression of the freezing point of carbon tetrachloride, that the molecular weight was of the order 153—156, a value approximately in agreement with the formula Cl_2O_6 ($M = 166·9$).

The results of Goodeve and Todd (*Nature*, 1933, **132**, 514) indicated that the oxide existed as ClO_3 in the vapour phase, and the magnetic measurements of Farquharson, Goodeve, and Richardson (*Trans. Faraday Soc.*, 1936, **32**, 790) showed that, in the solid and the liquid phase, an equilibrium existed between the two forms ClO_3 and Cl_2O_6.

In this work, the main physical properties of the oxide have been determined, and the heat of activation for the decomposition of the liquid measured.

EXPERIMENTAL.

Preparation.—The dichlorine hexoxide was prepared (cf. Schumacher and Stieger, *Z. anorg. Chem.*, 1929, **184**, 272) by mixing a stream of ozonised oxygen with a stream of oxygen containing chlorine dioxide. The apparatus, which consisted entirely of soda glass, is shown in Fig. 1. Taps which were not open to attack from chlorine dioxide were lubricated with Apiezon L grease. The others were lubricated with pure metaphosphoric acid of a suitably viscous consistency. Since the hexoxide reacts with all known lubricants and dissolves very readily in phosphoric acid (thereby being itself decomposed), no taps were placed beyond the mixing vessel *R* in which the hexoxide was formed.

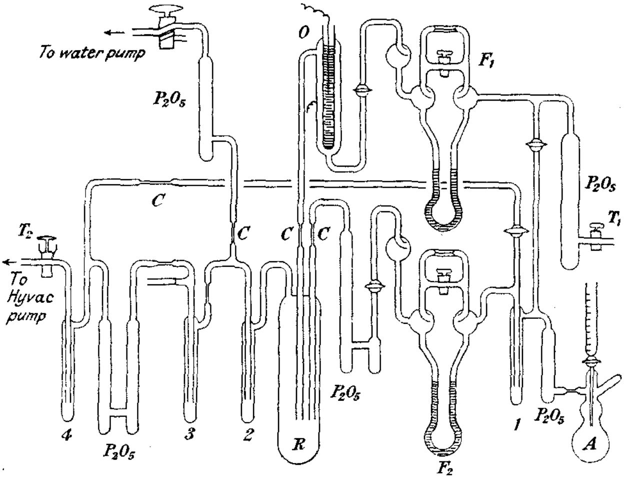
The chlorine dioxide was prepared by dropping concentrated sulphuric acid on powdered potassium chlorate cooled to − 78° in the vessel *A*. When all the acid had been added, the apparatus was evacuated with a Hyvac pump. The mixture was allowed to warm slowly, the temperature being so adjusted that the reaction proceeded gently. The dioxide was collected in trap 1, cooled in liquid air. The preparation vessel *A* was then sealed off at its constriction.

The Pyrex ozoniser *O* was of the vertical Siemens type; the inner tube was filled with copper

sulphate solution, and the outer one coated on the outside with colloidal graphite. The discharge was produced by A.C. of 10,000 volts and 350 cycles.

A stream of cylinder oxygen was passed at atmospheric pressure into the apparatus at T_1, and was divided into two parts, one passing through the ozoniser, and the other over the chlorine dioxide in trap 1, now cooled in melting ice. The ozone and chlorine dioxide concentrations were about 7% and 20% by volume, respectively. The flow speeds were measured by the flow-meters F_1 and F_2, and regulated so that they were roughly 20 l./hr. for the ozone stream and 2 l./hr. for the dioxide. The streams were mixed in the reaction chamber R, cooled in melting ice. A brown liquid condensed on the sides of the vessel, and to some extent in the tubes beyond. The waste gases passed to the water pump, tap T_2 being closed.

FIG. 1.



In one preparation three separate charges of potassium chlorate were used, since it was not considered safe to prepare more than about 5 c.c. of chlorine dioxide at a time. When the liquid hexoxide was allowed to drain completely from the walls of the reaction chamber after the initial preparation, crystalline hexoxide was subsequently deposited at 0°. When the preparations had been completed, the reaction vessel and the traps for distillation were isolated from the rest of the apparatus by sealing off all the constrictions marked C in the figure. The preparation did not yield a pure product, chlorine dioxide and heptoxide being found amongst the impurities.

Purification.—Pure samples of the hexoxide could not be obtained merely by distilling away the top fractions and keeping the oxide in the preparation vessel—a method apparently used by previous workers. This was due largely to the presence of a white involatile solid residue which remained in R after all the oxides had been distilled away. A similar residue has been obtained by other workers with chlorine dioxide—the formation being especially marked in glass vessels. Schumacher and Stieger (*loc. cit.*) suggested that the white deposit resulted from attack of the dioxide on the glass and consisted of Si_6Cl_{14}. No detailed analysis has yet been carried out.

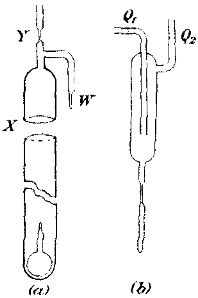
The oxide was, therefore, purified by fractional distillation. The reservoir R was kept at 6°, and the pure hexoxide was collected at − 20° in trap 3, the more volatile impurities passing over to a liquid-air trap 4. Trap 3 was sealed off and attached to any desired apparatus by means of the septum, thereby avoiding exposure of the oxide to the atmosphere.

Analysis.—The hexoxide was analysed by sealing about 0·1 c.c. in a small, thin-walled bulb. This was introduced into the Pyrex tube (Fig. 2*a*), which was in two portions as shown. These were sealed together at *X*. The tube was connected to a Hyvac pump and dried by heating with a yellow flame. (The bulb was moved to a cool part of the tube during this process.) The tube was then sealed off at the constriction *Y*. The small bulb was broken by shaking the tube, which was then heated with a blow-lamp flame, at first gently and finally strongly, in order to decompose the sample into oxygen and chlorine. After being heated for about 20 minutes, the tube was allowed to cool. The constriction *W* was opened under potassium iodide solution, which was drawn up into the tube. The chlorine was absorbed, and the iodine liberated was subsequently determined with sodium thiosulphate; the volume of the oxygen was measured directly. The chlorine : oxygen ratios obtained in this manner were 1 : 3·00 ± 0·03.

Melting Point.—Bodenstein, Harteck, and Padelt (*loc. cit.*) found the m. p. to be about − 1°, but Rollefson and Byrns (*J. Amer. Chem. Soc.*, 1934, **56**, 364) have prepared samples of hexoxide melting just above 0°. These were liquid at 0° in the presence of a few mm. of chlorine.

A quartz tube was constructed as shown in Fig. 2*b*, and connected to the apparatus by quartz-to-soda glass, graded joints, Q_1 and Q_2. It was heated with a blow-lamp flame under a vacuum to remove the last traces of moisture adsorbed on the walls, and a small quantity of hexoxide was condensed in it at − 20°. The oxide was then melted and allowed to run into the thin-walled, narrow-bore tube attached by the constriction to the bottom of the trap. As described below, dichlorine hexoxide decomposes into oxygen, chlorine, and the di- and hept-oxide at temperatures above − 20°. It was, therefore, necessary to carry out the above process under a high vacuum, and, when the oxide had drained into the thin tube, to cool in stages in order to allow evaporation of the volatile impurities from the crystals. When the temperature had reached − 78°, the tube was sealed off at the constriction. The m. p. was determined in the usual way, three values per sample being obtained with different rates of warming.

FIG. 2.



(*a*) (*b*)

Three different samples gave m. p.'s 3·50°, 3·52°, and 3·50°; the true m. p. is, therefore, 3·50°, with a maximum error of 0·05°.

On keeping one sample at 5·5° for 15 minutes, the m. p. fell by 0·2°; on keeping at 17° for 7 minutes there was a further fall of 0·45°. This indicates the ease with which thermal decomposition takes place.

It was not possible to obtain reproducible results for different samples when glass was employed instead of quartz. When the hexoxide was run into glass m. p. tubes and then distilled away, there remained on the walls a white deposit similar to that referred to above.

The colour of the hexoxide, as well as the m. p., was markedly affected by small quantities of impurity. When the oxide was pure it possessed a bright orange-red colour at − 78° and was pale yellow at − 180°. At low temperatures the colour of an impure sample was dark brown.

Vapour Pressure.—A measurement of the vapour pressure was first attempted by Bodenstein, Harteck, and Padelt (*loc. cit.*), who obtained a value of about 1 mm. of mercury at room temperature. Schumacher and Stieger (*loc. cit.*) obtained the rough values 1 mm. at 20° and 5—10 mm. at 40°, and Norrish and Neville (*Nature*, 1933, **131**, 544) found a value somewhat less than 1 mm. at 0°. Rollefson and Byrns (*loc. cit.*) made two measurements with an accuracy of about 10%: their results are indicated in Fig. 4 by " R. and B."

Measurement. The pressure-measuring apparatus was constructed as shown diagrammatically in Fig. 3. This consisted of a quartz spiral Bodenstein (Bourdon) gauge *G*, fitted with a mirror which reflected light from a source *S* about 1 m. distant into a photo-cell device *P*, a similar distance away. The lenses and slit of the optical system are not shown. The Bodenstein gauge was used with its outer jacket evacuated; the pressure in the spiral was determined by measuring the position of the reflected light beam with the photo-cell arrangement. The light source was a 15-c.p. filament lamp connected to a constant-voltage supply. The photo-cell device consisted of two separate selenium cells set up side by side and opposed in parallel as recommended by Hill (*Nature*, 1934, **134**, 289) and by Wood (*Rev. Sci. Instr.*, 1934, **5**, 295). The cells were connected to a Zernicke galvanometer, and screened from all light other than that reflected from the gauge mirror. They were further protected from local variations of temperature, to which they were susceptible, by means of suitable screens. The pair of cells was mounted

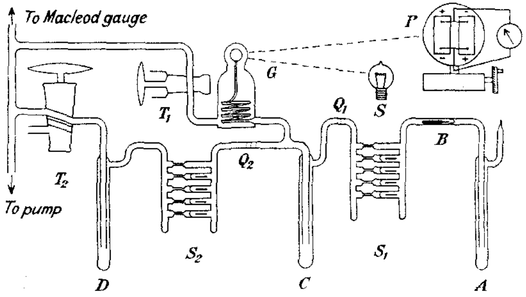
on the carriage of a Hilger travelling micrometer, graduated in 0·01 mm. divisions and readable to 0·1 division. Readings of the micrometer were taken when, on illumination of the cells, there was no deflection of the galvanometer, *i.e.*, when the cells were equally illuminated. Their position, therefore, marked the centre of the reflected light spot. The gauge was calibrated against a wide-bore mercury manometer and a Macleod gauge. A pressure equivalent to 1 mm. of mercury in the spiral of the gauge caused a deflection of the light spot of 0·412 mm.

If the photo-cells had been perfectly uniform and matched, vibration of the pressure-gauge mirror, being of a very much higher frequency than the period of the galvanometer, would not have affected the zero position. As this was not altogether the case, it was necessary to set the entire apparatus on a special bench mounted on six old tennis balls. Under favourable conditions pressures could be measured to within 0·01 mm. of mercury.

The trap A, containing the hexoxide, was sealed to the rest of the apparatus at B. S_1 and S_2 are banks of septa, and Q_1 and Q_2 graded quartz-to-soda glass seals. The septa were broken with magnetically operated hammers. C is a quartz trap, and D a waste trap cooled in liquid air. The taps T_1 and T_2 did not come into contact with the hexoxide, and were lubricated with Apiezon L grease.

About 0·05 c.c. of hexoxide was distilled into C after the septum at B had been opened. Both traps were then cooled to − 78°, and S_1 closed by sealing a constriction. The entire

Fig. 3.



apparatus was evacuated to 0·003 mm., and the bank of septa S_2 and the tap T_1 closed. Measurements of the vapour pressure of the sample in C were then made. The temperature was adjusted by immersing C in cooled alcohol, the temperature of which was measured with a calibrated thermometer. Below 0° the rate of decomposition of the sample was negligible, and the vapour pressure was measured directly. At temperatures where the liquid was decomposing, pressure readings were taken every 2 minutes until the pressure increased uniformly with time. The true vapour pressure was determined by plotting the results and extrapolating the pressure–time curve to zero time.

It was not possible to obtain reproducible values of the vapour pressure when large quantities of hexoxide (1 c.c.) were used. This was due to the impossibility of removing the last traces of volatile impurity (formed by thermal decomposition of the liquid, see p. 296), which was entangled in the bulk of the hexoxide when it was solidified. At temperatures above − 180° these impurities diffused slowly into the gas phase where they registered a small variable pressure. When a small crystal of hexoxide was used, the error due to this effect was negligible in comparison with the vapour pressure of the oxide, and the results were reproducible for different samples. The use of a small crystal at the higher temperature was also an advantage, as the effect of thermal decomposition was very much reduced. At temperatures below 0° the values for the vapour pressure were probably accurate to 0·02 mm. At temperatures above this the limit of error increased with the rate of decomposition of the hexoxide. Below 0° the error in absolute temperature was about 0·5°; above 0°, 0·2°.

Results. The results for three different samples are shown plotted on the usual logarithmic

scale in Fig. 4. The values for the liquid and for the solid lie on two straight lines, the equations for which are:

$$\text{Liquid, } \log_{10} p_{mm.} = -2070/T + 7{\cdot}1 \quad (1)$$
$$\text{Solid, } \log_{10} p_{mm.} = -2690/T + 9{\cdot}3 \quad (2)$$

These lead to values for the latent heat of evaporation and of sublimation of 9·5 ± 1 and 12·3 ± 0·5 kg.-cals. per g.-mol. respectively. It is seen that, in spite of the association to hexoxide in the liquid phase, the constant in equation (1) has the normal value of about 7·5 (Trouton's rule). This may be due to the small heat of dissociation (cf. Farquharson, Goodeve, and Richardson, *loc. cit.*) for the hexoxide molecule:

$$Cl_2O_6 \text{ (liquid)} \longrightarrow 2ClO_3 \text{ (liquid)}; \ \Delta U = +1{,}700 \pm 500 \text{ cals.}$$

FIG. 4.

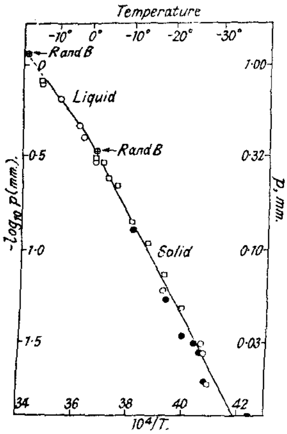
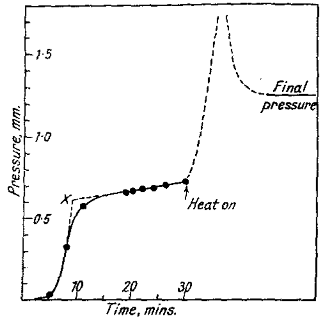


FIG. 5.



Decomposition of Liquid Hexoxide.—Norrish and Neville (*loc. cit.*) found a temperature coefficient of 2·34 per 10° for the thermal decomposition of the liquid oxide. Byrns and Rollefson (*J. Amer. Chem. Soc.*, 1934, **56**, 2245), from measurements of the temperature coefficient, have obtained a value of 21—26 kg.-cals. for the heat of activation.

A value for the heat of activation for the decomposition of the liquid can be calculated from the Arrhenius equation, the velocity constant for the reaction being taken as proportional to the rate of pressure increase. The pressure–time curves at 4·8°, 10·0°, and 14·8° lead to a value of 22 ± 2 kg.-cals., which corresponds to a temperature coefficient of 3·8 per 10°. This is in agreement with the value determined by Byrns and Rollefson (*loc. cit.*). They assumed that this value represents the heat of activation for the reaction $ClO_3 \longrightarrow ClO_2 + \frac{1}{2}O_2$. Since the liquid exists almost entirely as hexoxide, and since we have found that chlorine and dichlorine heptoxide, as well as chlorine dioxide and oxygen, are formed in the liquid decomposition, it is impossible to state exactly what the equation may be. The decomposition may, however, occur through the trioxide present in the equilibrium mixture.

Molecular Constitution and Decomposition in the Vapour Phase.—This investigation was carried out in order to verify the previous work of Goodeve and Todd (*loc. cit.*), who showed that the molecular weight in the vapour phase corresponded to the formula ClO_3; the pressures mentioned in their note are, however, greater than the vapour pressures at room temperature.

Measurement. Some chlorine hexoxide was sealed in a small trap, which was connected to a 54-cm. quartz tube with end windows, and to the Bodenstein pressure gauge used for the vapour-

pressure measurements. About half of the oxide was distilled away, leaving only enough to fill the apparatus to about 1 mm. pressure or less. Thus no liquid remained unevaporated when the small trap was warmed to room temperature. Pressure readings were taken as soon as the cooling mixture (– 78°) was removed, and were continued until the rate of pressure increase became constant. The absorption spectrum was photographed through the tube at intervals. The tube was then heated with a hand blow-pipe to decompose the oxide vapour to oxygen and chlorine. The tube was heated and cooled alternately until the pressure in the system at room temperature reached a constant value and there was no evidence of oxides of chlorine in the absorption spectrum. The final pressure was then measured and assumed to be due to the oxygen and chlorine formed by decomposition.

Results. Fig. 5 shows a typical pressure–time curve. It is seeen that no constant initial pressure was reached, but that as soon as the oxide had evaporated the rate of increase of pressure became approximately constant. The pressure of the oxide vapour, corresponding to the amount of hexoxide initially present, was determined by extrapolation of the pressure–time curve to the point X in the graph. Four experiments were carried out. The results are given below :

Initial press. (mm.) extrapolated	1·13	0·73	0·62	0·25
Final pressure	2·29	1·45	1·25	0·48
Ratio	2·03	1·97	2·04	1·95

These results show conclusively that the oxide exists almost entirely, if not completely, as ClO_3 in the vapour phase, the total decomposition being represented by the equation :

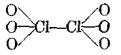
$$\begin{array}{ccc} ClO_3 & \longrightarrow & \tfrac{1}{2}Cl_2 + \tfrac{3}{2}O_2 \\ 1\ \text{vol.} & \rightarrow & 2\ \text{vols.} \end{array}$$

The higher pressures found in the previous work (Goodeve and Todd, *loc. cit.*) may have been due to a faulty calibration of the pressure gauge.

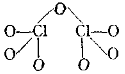
The photographs of the absorption spectrum showed that the continuous absorption due to ClO_3 decreased with time at room temperatures after the tube had been filled, whereas the band absorption due to the dioxide increased in intensity.

Discussion.

The physical properties of dichlorine hexoxide are compared with those of the other oxides in the table. It is of interest to note that this oxide has the highest melting point, the highest density, and the highest latent heat of evaporation (lowest vapour pressure). The contrast is particularly striking when it is compared with the heptoxide. A sym-



(non-planar).



(non-planar).

metrical structure for the hexoxide and an unsymmetrical one for the heptoxide would explain these differences. The symmetrical molecules could form crystals more easily, pack

Oxide.	Cl_2O.	ClO_2.	Cl_2O_6.	Cl_2O_7.
Mol. wt.	87	67·5	167	183
M. p.	–116° *	–59° †	+3·5°	–91·5° ‖
B. p.	2° *	11·0° †	203° (calc.)	80° ‖
Latent heat of evaptn., kg.-cals.	6·20 *	6·52 †	9·50	8·29 ‖
Trouton's const.	22·5 *	23·0 †	21	23·4 ‖
Vap. press., mm. at 0°	699 *	490 †	0·31	23·7 ‖
Density	—	1·64, 0° ‡	2·02, 3·5° §	1·86, 0° ¶
G.-mol. vol., c.c.	—	41·1	82·7	98·4

* Goodeve, J., 1930, 2733. † King and Partington, J., 1926, 925. ‡ Cheesman, J., 1930, 36. § Farquharson, Goodeve, and Richardson, *loc. cit.* ‖ Goodeve and Powney, J., 1932, 2078. ¶ Private communication from Mr. A. E. L. Marsh.

closer together, and thus have a larger latent heat of evaporation. They would, therefore, have a higher melting point, density, and latent heat than the unsymmetrical molecules. An exactly parallel relation is seen when these properties for the aliphatic alcohols are contrasted with the corresponding properties for the isomeric ethers. The latter are more

unsymmetrical than the former (as they possess a central oxygen atom with a valency angle of about 126°) and they have very much lower melting points, densities, etc.

Dichlorine hexoxide has been found to be the least explosive of all the known oxides of chlorine. It does not explode with shock or sudden heat, although it may do so on contact with water or organic matter. It is, however, the least thermally stable of the oxides, and decomposes very readily in the liquid or the vapour phase at room temperature.

At the same time the authors' experiences with this and other oxides of chlorine have shown that *there are no safe conditions* under which they can be handled. Elaborate precautions against harm arising from explosions have only partly succeeded in preventing personal injuries.

SUMMARY.

The preparation of dichlorine hexoxide from chlorine dioxide and ozone, and its purification and analysis have been described.

The melting point has been determined as 3·50° ± 0·05°. The vapour pressure has been measured over a temperature range − 40° to + 20°. The values for the latent heats of evaporation and sublimation have been calculated from these results.

The heat of activation for the decomposition of the liquid has been found to be 22 ± 2 kg.-cals. The oxide has been shown to exist in the vapour phase as ClO_3, which decomposes readily into dioxide and oxygen.

The physical properties of the hexoxide have been contrasted with those of the other oxides of chlorine, and the structures of it and of the heptoxide have been discussed.

The authors are indebted to the Department of Scientific and Industrial Research for a grant in aid of this research.

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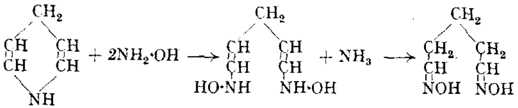
61. *The Preparation of 1 : 5-Dioximes from Pyridine Bases.*

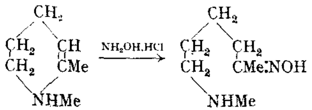
By BRIAN DUNCAN SHAW.

IN a previous communication (J., 1925, **127**, 215) it was shown that glutardialdoxime may be prepared from pyridine by treatment with hydroxylamine after reduction of the base to the dihydro-stage. This reaction is now shown to be a general one for the pyridine series, dioximes having been obtained from the following bases: pyridine, α-picoline, nicotine, *2-styrylpyridine*, *4-styrylpyridine*, *2 : 4 : 6-trimethylpyridine*, *2-methyl-5-ethylpyridine*, 2-benzylpyridine, and 2-β-phenylethylpyridine.

The course of the reaction is believed to be as follows:



(I.)



(II.)

This view is supported by the known conversion of 1-methyl-Δ^1-pipecoleine (I) into the oxime of methyl δ-methylaminobutyl ketone by the action of hydroxylamine hydrochloride (Lipp and Widnmann, *Ber.*, 1905, **38**, 2473).

None of the oximes other than glutardialdoxime have been obtained as solids except at

low temperature; they are thick, almost colourless glues which yield glass-like solids which can be powdered when cooled in solid carbon dioxide–acetone, but revert to the semi-liquid state at room temperature and fail to crystallise on standing during several years. As this failure to crystallise might be due to impurity in the original bases, a simple but effective method was developed for the purification of 2 : 4 : 6-trimethylpyridine, the oxime was distilled in a vacuum, converted into the diketone, and the dioxime regenerated from this; the product was still a glue. The bis-2 : 4-dinitrophenylhydrazones, however, are solids which can be crystallised from alcohol, although very sparingly soluble. They are formed slowly from the oximes by treatment with 2 : 4-dinitrophenylhydrazine in dilute hydrochloric acid, or more rapidly from the free 1 : 5-dicarbonyl compounds. The latter are readily obtained by treating the dioximes with sodium nitrite in cold acid solution. Those from bases having an unsubstituted 2-position give colours with Schiff's reagent and reduce Fehling's solution.

Glutardialdoxime regenerates pyridine when boiled with concentrated hydrochloric acid, but in poor yield and with formation of much tar. The mechanism of the reaction is obscure, but the first stage is undoubtedly elimination of one molecule of hydroxylamine. In the cold the reaction ceases at this stage; the resulting red fluorescent solution turns yellow with alkali in the cold. The alkaline solution slowly turns red when heated, but reverts to yellow when cooled. These changes can be repeated indefinitely.

The pyridine nucleus in 2-styrylpyridine is more easily reduced than the ethylenic linkage in the side chain when sodium and ethyl alcohol are used. With amyl alcohol and with acid reducing agents the reverse is the case.

EXPERIMENTAL.

Drying of Alcohol.—A small percentage of water in the alcohol seriously reduces the yield owing to hydrolysis of the dihydropyridine (J., 1924, **125**, 3041). Boiling with calcium carbide is the most effective and economical process, but necessitates pulverisation of the drying agent, and the product has a highly unpleasant odour. These disadvantages are avoided by using a simple apparatus which the author has found satisfactory during the past eleven years. Its efficiency is due to the greater volatility, as compared with anhydrous alcohol, of the constant-boiling mixture of alcohol and water, as a result of which the moisture is concentrated on the surface of the drying agent.

A metal boiler is surmounted by a glass tube, 1 m. long and 3 cm. internal diameter, fitted with a double-surface reflux condenser. The tube is packed with calcium carbide broken to the size of Brazil nuts; the finer material obtained in breaking the calcium carbide is put into the boiler. The lime produced is washed down by the refluxing liquid. As the gases are produced in contact with only a small proportion of alcohol, the product has no unpleasant odour. Drying is complete when bubbles can no longer be seen, with a magnifying glass, on the surface of the lumps of calcium carbide. The product is distilled from the lime. By this method 5 l. of 96% alcohol may be completely dried in 12 hours. If the process be prolonged, a yellow solution results from which crystals of calcium ethoxide separate on cooling. Although the azeotropic mixture method of drying alcohol is inconvenient in ordinary laboratory practice, it is valuable for ensuring the dryness of alcohol used in the method described, when the alcohol has been stored in an ordinary bottle for any length of time. For this purpose the alcohol is mixed with 10% by volume of dry benzene and distilled through a fractionating column until 15% of the mixture has been removed. The residue is used for the reduction.

General Method.—The pyridine base (1 mol.) is reduced with sodium (1 atom) and boiling, dry ethyl alcohol. The cooled solution is treated with hydroxylamine hydrochloride (0·5 mol.) dissolved in the minimum quantity of warm water, followed as rapidly as possible by concentrated hydrochloric acid (0·5 mol.) diluted with twice its volume of alcohol (96%). The mixture is boiled until the evolution of ammonia slackens (1 hour), filtered, and the alcohol removed. The oxime is extracted from the residue with a 10 or 20% solution of sodium hydroxide, the solution washed with ether and neutralised, the oxime extracted with ether, the solvent removed, and the product dried in a vacuum. The yields, allowing for recovered base, exceed 90% of the theoretical. When the filtered alcoholic solution is allowed to stand overnight, a small quantity of sodium chloride is deposited in well-defined needles, ½—1 cm. in length.

Amyl alcohol may be substituted for ethyl: in this case the quantity of sodium is halved and the hydrochloric acid omitted, since, whereas with ethyl alcohol approximately half the

hydrogen escapes, with amyl alcohol it is almost completely absorbed. An alcoholic solution of hydroxylamine hydrochloride is necessary, however, as otherwise the yield is reduced owing to hydrolysis of the dihydropyridine. Details of variations with particular bases are given in the sequel.

Pyridine.—The solution from pyridine (80 g.), sodium (23 g.), alcohol (350 c.c.), hydroxylamine hydrochloride (35 g.), and concentrated hydrochloric acid (50 c.c.), after removal of sodium chloride, was distilled until approx. 100 c.c. remained. On standing overnight, glutardialdoxime crystallised; it was pure after washing with water to remove sodium chloride. Yield, 27 g., m. p. 175°. *Glutardialdehydebis-2 : 4-dinitrophenylhydrazone* has m. p. 169—172° (Found: N, 24·3. $C_{17}H_{16}O_8N_8$ requires N, 24·35%).

Action of Hydrochloric Acid on Glutardialdoxime.—The oxime (26 g.) was warmed with 18% hydrochloric acid (100 c.c.). A vigorous reaction set in and the solution turned dark brown. Basification and distillation yielded pyridine (4 g.; 20% of the theoretical quantity) and a residue of tar. The purity of the base was established by complete conversion of a sample into the methiodide, m. p. 117° without purification. Modifications failed to improve the yield.

The oxime (13 g.) was added to cold concentrated hydrochloric acid (25 c.c.), and the solution kept in a vacuum over sulphuric acid. Pure hydroxylamine hydrochloride commenced to separate at once, and continued during 7 days; yield, 6·5 g. (93% of the theoretical for 1 mol.). The viscous filtrate was completely soluble in water and showed the curious colour changes already described; when heated, it gave pyridine and tar as before.

2-*Picoline.*—The oxime was not readily soluble in ether; it was therefore washed by decantation and dissolved in alcohol, and the alcohol removed in a vacuum. *δ-Acetobutaldehydebis-2 : 4-dinitrophenylhydrazone* has m. p. 129° (Found: N, 23·7. $C_{18}H_{18}O_8N_8$ requires N, 23·6%).

2 : 4 : 6-*Trimethylpyridine.*—The product of condensation of acetone, paraldehyde, and ammonia was fractionated, and the portion, b. p. 169—175°, mixed with the theoretical quantity of nitric acid (d 1·42); the *nitrate* separated at once on cooling and was recrystallised from alcohol, m. p. 199° (decomp.) (Found: *M* by titration, 185. $C_8H_{11}N,HNO_3$ requires *M*, 184). The base had b. p. 169·2—169·4°/760 mm., $d_{17^\circ}^{17^\circ}$ 0·9166. *αγ-Diacetyl-β-methylpropanedioxime* had b. p. 275°/12 mm. (Found: N, 16·1. $C_8H_{16}O_2N_2$ requires N, 16·3%), and the *bis-2 : 4-dinitrophenylhydrazone*, m. p. 197—199° (Found: N, 22·5. $C_{20}H_{22}O_8N_8$ requires N, 22·3%).

2-*Styrylpyridine.*—From the base (66 g.), sodium (9 g.), alcohol (135 c.c.), and hydroxylamine hydrochloride (15 g.) there was obtained *ω-aldehydo-γ-keto-α-phenyl-Δ^α-hexenedioxime* (9·6 g.) (Found: C, 66·7; H, 7·6; N, 11·8. $C_{13}H_{16}O_2N_2$ requires C, 66·9; H, 7·3; N, 12·0%). 57 G. of base were recovered. The *bis-2 : 4-dinitrophenylhydrazone* had m. p. 55—59° (Found: N, 19·4. $C_{25}H_{22}O_8N_8$ requires N, 19·9%).

The author is indebted to the Chemical Society for a grant.

UNIVERSITY COLLEGE, NOTTINGHAM. [*Received, December 4th*, 1936.]

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62. *Studies in the Sterol Group. Part XXVIII. The Application of the Reformatsky Reaction to 7-Ketocholesteryl Acetate: Δ⁵-Cholestene-3 : 7-diol-7-acetic Acid.*

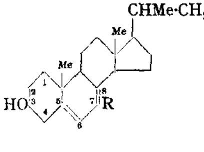
By E. R. H. JONES and F. S. SPRING.

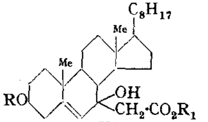
IN Part XXVI an attempt was made to prepare a derivative of 7-dehydrocholesterol (I, R = H) by the action of methylmagnesium iodide upon 7-ketocholesteryl acetate. The reaction, however, gave 7-methylenecholesterol (Bann, Heilbron, and Spring, J., 1936, 1274) and not the desired 7-dehydro-7-methylcholesterol (I, R = Me). With the same object in view, the Reformatsky reaction has now been applied to 7-ketocholesteryl acetate.

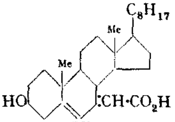
Treatment of 7-ketocholesteryl acetate with ethyl bromoacetate in the presence of zinc gives a mixture from which Δ^5-cholestene-3 : 7-diol-7-acetic acid (II, R = R_1 = H), m. p. 161° (decomp.), is isolated, characterised by its *methyl* ester (II, R = H; R_1 = Me), m. p. 161—161·5°, and by the *3-monoacetate* (II, R = Ac; R_1 = Me), m. p. 136°, and the *3-monobenzoate* (II, R = Bz; R_1 = Me), m. p. 158°, of the latter.

Although various methods of dehydration have been applied to (II, R = R′ = H), loss of water is invariably effected with the formation of an exocyclic ethenoid linkage. Whereas

distillation of Δ^5-cholestene-3 : 7-diol-7-acetic acid in high vacuum results in severe decomposition, the 3-monobenzoate and the 3-monoacetate of the methyl ester distil unchanged, a result which is surprising in view of the facile dehydration of 7-hydroxy-7-methylcholesteryl benzoate by this method (Bann, Heilbron, and Spring, *loc. cit.*).


(I.)


(II.)


(III.)

On refluxing Δ^5-cholestene-3 : 7-diol-7-acetic acid with acetic anhydride, 7-methylenecholesterol is obtained, dehydration having been accompanied by decarboxylation. The intermediate stage in this reaction is realised by treatment of Δ^5-cholestene-3 : 7-diol-7-acetic acid with acetic anhydride in pyridine solution; *3-acetoxy-Δ^5-cholestenylidene-7-acetic acid* (III), m. p. 216—217° (decomp.), is then isolated. Its ultra-violet absorption spectrum (broad band, max. 2680A., log $\varepsilon = 4{\cdot}16$) is in harmony with the proposed structure. If the acid had the alternative conjugated system ($C_{5:6}$—$C_{7:8}$), it would be expected to exhibit the typical absorption spectrum of ergosterol, since the carboxyl group would not be conjugated with the chromophore.

EXPERIMENTAL.

Δ^5-Cholestene-3 : 7-diol-7-acetic Acid.—A mixture of 7-ketocholesteryl acetate (12 g.), ethyl bromoacetate (10 g.), zinc (4 g.), and dry benzene (100 c.c.) was heated on the steam-bath. Cooling was necessary to modify the vigour of the initial reaction, after the cessation of which the mixture was heated under reflux for 6 hours. The cooled mixture was treated with dilute sulphuric acid, the benzene layer washed with water and dried, and the benzene removed. The residual gum, which would not crystallise, was hydrolysed by standing at room temperature for 5 days with a solution of potassium hydroxide (12 g.) in methyl alcohol (100 c.c.). After the addition of ice and dilute hydrochloric acid the mixture was extracted with ether, and the extract washed with water. The acid product was isolated by shaking with aqueous sodium carbonate, acidification producing a tacky solid. Crystallisation was effected from ether–petrol (b. p. 80—100°), from which Δ^5-cholestene-3 : 7-diol-7-acetic acid (3·5 g.) separated in lustrous plates, m. p. 161° (decomp.). With the antimony trichloride reagent, the acid gives an intense royal-blue coloration; $[\alpha]_D^{20°} - 30{\cdot}3°$ ($l = 1$, $c = 1{\cdot}15$ in chloroform). In spite of prolonged desiccation it was not possible to obtain the acid free from solvent. The methyl ester (II, R = H; R_1 = Me), prepared by means of diazomethane, was crystallised from acetone–petrol (b. p. 60—80°) and twice from aqueous methyl alcohol, from which *methyl Δ^5-cholestene-3 : 7-diol-7-acetate* separated in large plates, m. p. 161—161·5°. With the antimony trichloride reagent it gives a green coloration which gradually changes to blue; $[\alpha]_D^{20°} - 49{\cdot}1°$ ($l = 1$, $c = 2{\cdot}52$ in chloroform) (Found: C, 75·9; H, 10·4. $C_{30}H_{50}O_4$ requires C, 75·9; H, 10·6%). *Methyl 3-acetoxy-Δ^5-cholesten-7-ol-7-acetate* (II, R = Ac; R_1 = Me) was prepared by refluxing the methyl ester (0·1 g.) with acetic anhydride (1·5 c.c.) and anhydrous sodium acetate (0·05 g.) for 10 minutes. The solid isolated by water precipitation was crystallised twice from methyl alcohol, from which the acetate separated in fine needles, m. p. 136°; with the antimony trichloride reagent it gives a greenish-blue coloration; $[\alpha]_D^{20°} - 62{\cdot}3°$ ($l = 1$, $c = 0{\cdot}69$ in chloroform) (Found: C, 74·4; H, 9·9. $C_{32}H_{52}O_5$ requires C, 74·4; H, 10·1%). *Methyl 3-benzoyloxy-Δ^5-cholesten-7-ol-7-acetate* (II, R = Bz; R_1 = Me). A solution of the methyl ester (0·1 g.) in pyridine (1 c.c.) and benzoyl chloride (0·4 g.) was set aside at room temperature for 18 hours. The oily mixture was washed with water, and the residue triturated with cold methyl alcohol and crystallised from acetone–methyl alcohol, from which the benzoate separated in fine needles, m. p. 158°. With the antimony trichloride reagent it gives a green coloration; $[\alpha]_D^{20°} - 14°$ ($l = 1$; $c = 0{\cdot}43$ in chloroform) (Found: C, 76·7; H, 9·4. $C_{37}H_{54}O_5$ requires C, 76·8; H, 9·4%).

7-Methylenecholesterol.—A solution of Δ^5-cholestene-3 : 7-diol-7-acetic acid (0·3 g.) in acetic anhydride (4 c.c.) was heated under reflux for 4 hours; the product obtained by addition of

water was isolated by means of ether, and the extract washed with aqueous sodium carbonate. Removal of the solvent gave a gum, which could not be crystallised. It was hydrolysed by refluxing for 30 minutes on the steam-bath with methyl-alcoholic potassium hydroxide (5 c.c., 5%); treatment with water and ether extraction then yielded a semi-solid mass. This was benzoylated with pyridine (0·8 c.c.) and benzoyl chloride (0·1 g.) by standing at room temperature for 24 hours. The reaction mixture was lixiviated with water and the solid produced on grinding the oily residue with methyl alcohol was crystallised twice from acetone, giving 7-*methylenecholesteryl benzoate*, m. p. 141°, either alone or in admixture with an authentic specimen.

3-*Acetoxy*-Δ^5-*cholestenylidene*-7-*acetic Acid*.—A mixtue of Δ^5-cholestene-3 : 7-diol-7-acetic acid (0·3 g.), pyridine (3 g.), and acetic anhydride (3 g.) was heated on the steam-bath for 30 minutes. On pouring into water an oil separated which solidified on standing at 0° overnight. Crystallisation first from petrol (b. p. 60—80°) and then from methyl alcohol gave 3-*acetoxy*-Δ^5-*cholestenylidene*-7-*acetic acid* (0·1 g.) in aggregates of small prisms, m. p. 216—217° (decomp.). The acid can be extracted from an ethereal solution with aqueous sodium carbonate. It sublimes unchanged in a high vacuum and with the antimony trichloride reagent produces a green coloration which gradually turns to blue; $[\alpha]_D^{20°}$ – 334·6° (l = 1, c = 1·93 in chloroform) (Found: C, 76·7; H, 10·1. $C_{31}H_{48}O_4$ requires C, 76·8; H, 10·0%).

The authors' thanks are due to Professor I. M. Heilbron, F.R.S., for his interest in this work, to the University of Wales for a Fellowship, and to the Rockefeller Foundation for a grant.

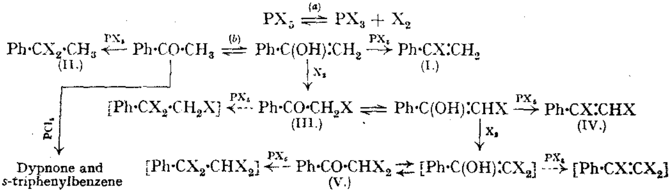
THE UNIVERSITY, MANCHESTER. [*Received, December 8th*, 1936.]

63. *The Action of Phosphorus Pentahalides on Acetophenone.*

By WILLIAM TAYLOR.

AN attempt to prepare αα-dibromoethylbenzene, required for kinetic purposes, by adding acetophenone to phosphorus trichlorodibromide gave a liquid having almost the required bromine content. Preliminary kinetic experiments with alcoholic potassium hydroxide, however, revealed a non-equivalent rapid reaction, followed by a much slower halogen elimination. Oxidation of the liquid with alkaline permanganate gave benzoic acid alone and therefore the slowly reacting halogen was not nuclear. End-product experiments yielded no acetophenone or its acetal and the only product identified was a small amount of a mixture of the α- and the β-form of "bromodiphenacyl." This had previously been obtained from ω-bromoacetophenone (*e.g.*, Fritz, *Ber.*, 1895, **28**, 3088; Paal and Demeler, *Ber.*, 1896, **29**, 2093) and its formation suggested that ω-bromoacetophenone was present in the liquid. When phosphorus trichlorodibromide was added to well-cooled acetophenone, the product was mainly ω-bromoacetophenone.

At this point it was decided to examine more closely the action of phosphorus pentahalides, and especially of the chlorobromide, on acetophenone. The results can be summarised and interpreted by the following scheme:



Compounds and reactions indicated by dotted lines were not realised in practice. Two feasible assumptions have been made, namely, that halogen substitution for ketonic oxygen or for hydroxyl is effected by the pentahalide (in preference to the trihalide while the former

is still present), and that halogen addition to the enolic form is effected by free halogen (followed by the elimination of hydrogen halide). The main evidence on which the scheme is based is the isolation or identification of compounds of types (I), (II), (III), (IV), and (V), but further support is given by the following considerations. The proportion of (III) formed relative to (I) and (II) will be governed mainly by the equilibria (*a*) and (*b*): these are both affected by temperature, and (*b*) by the presence of acid (HX) also. However, the effect of (*b*) will be more or less constant, because acetophenone is always one of the two reagents. On the other hand the nature of the reagent PX_5 varies with the nature of X, and with this will vary the position of (*a*). Thus one need only discuss the effect of (*a*). At any temperature the degree of dissociation of the trichlorodibromide will be greater than that of the pentachloride, and hence one would expect that at relatively low temperatures the proportion of (III) produced by the former would be greater than that produced by the latter. This is in agreement with practice, for, whilst the main product with phosphorus chlorobromide was ω-bromoacetophenone (III), Friedel (*Compt. rend.*, 1868, **67**, 1192) and the present author obtained only α-chlorostyrene (I) and αα-dichloroethylbenzene (II) with phosphorus pentachloride. The scheme now presented differs materially from the one advocated by the earlier investigators (cf. Dyckerhoff, *Ber.*, 1877, **10**, 120) and still quoted (*e.g.*, Francis, "Notes on Organic Chemistry," 1935, p. 322):

$$Ph{\cdot}CO{\cdot}CH_3 \xrightarrow{PCl_5} \underset{\text{(unstable intermediate)}}{Ph{\cdot}CCl_2{\cdot}CH_3} \xrightarrow{-HCl} Ph{\cdot}CCl{:}CH_2$$

It would appear that the instability previously attributed to the "keto-halides" of acetophenone is due to the *simultaneous* and not subsequent formation of α-halogenostyrene.

The products formed by adding acetophenone to well-cooled phosphorus chlorobromide were mainly ω-bromoacetophenone and αβ-dibromostyrene, together with ωω-dibromoacetophenone and αα-dibromoethylbenzene in smaller amounts. In all probability α-bromostyrene also was formed, but was reconverted into acetophenone during the subsequent treatment (Ashworth and Burkhardt, J., 1928, 1791, have shown its almost instantaneous transformation into acetophenone by boiling formic acid). Kröhnke (*Ber.*, 1936, **69**, 921) found that the difficulty in preparing ωω-dibromo- and ωωω-tribromo-acetophenone from bromine and acetophenone was due to the ready reduction of these compounds by acetophenone in the presence of hydrogen bromide. This affords an explanation of the small amount of di- relative to mono-bromoacetophenone produced under the conditions of the present experiments with phosphorus chlorobromide, especially when this is added to acetophenone and not vice versa. Excess of phosphorus chlorobromide gave with ω-bromoacetophenone a mixture of ωω-dibromoacetophenone and αβ-dibromostyrene. Phosphorus pentabromide reacted vigorously with acetophenone to give much carbon and traces only of ω-bromoacetophenone. Phosphorus pentachloride and acetophenone yielded αα-dichloroethylbenzene and α-chlorostyrene (compare Friedel, *loc. cit.*). Phosphorus pentachloride, or the hydrogen chloride liberated in the reaction, acted also as a condensing agent, for in one experiment, acetophenone and the pentachloride being in contact for many hours at room temperature, dypnone was formed (compare Béhal, *Bull. Soc. chim.*, 1888, **50**, 632; Dyckerhoff, *loc. cit.*).

Experimental.

Preparations.—αβ-Dibromostyrene obtained from phenylacetylene (Hessler, "Organic Syntheses," 1922, **2**, 67) by addition of bromine (Nef, *Annalen*, 1899, **308**, 223) had b. p. 136—138°/17 mm. (Nef gives b. p. 132—135°/15 mm.).

ω-Bromoacetophenone prepared by Rather and Reid's method (*J. Amer. Chem. Soc.*, 1919, **41**, 75) had b. p. 138—139°/14 mm., m. p. 50° (Clibbens and Nierenstein, J., 1912, **107**, 1492, give b. p. 135°/18 mm.).

ωω-Dibromoacetophenone was prepared from acetophenone (20 g.) in glacial acetic acid (25 c.c.) at 35—40° by the addition of bromine (60 g.) in glacial acetic acid (30 c.c.) during 15 minutes. After being left at room temperature for 1½ hours, the liquid was poured into ice-water (500 c.c.), and the product crystallised from methylated spirit (40 c.c.); yield 25 g., b. p. 159—160°/13 mm., m. p. 36—37° (Evans and Parkinson, *J. Amer. Chem. Soc.*, 1913, **35**, 1771, give b. p. 175—176°/23 mm.) (Found: Br, 57·6. Calc.: Br, 57·6%).

Reaction between Acetophenone and Phosphorus Chlorobromide.—Acetophenone (60 g.) was added (about 2 drops per sec.) with shaking during 1 hour to phosphorus chlorobromide (150 g.), surrounded by ice-water: there was a vigorous evolution of hydrogen bromide and the temperature never rose above 5°. The liquid was then heated at 40° for ¼ hour, cooled, added to ice (500 c.c.), left 1 hour, and extracted with ether. Five fractions were obtained by distillation: (1) 10·8 g., b. p. 80—90°/15 mm. (Found: Br, 15·9%); (2) 8·6 g., b. p. 90—105°/15 mm. (Found: Br, 21·3%); (3) 11·5 g., b. p. 105—125°/15 mm. (Found: Br, 31·4%); (4) 21·5 g., b. p. 125—135°/12 mm. (Found: Br, 53·7%); (5) 23·5 g., b. p. 135—158°/12 mm. (Found: Br, 59·3%). Much tar was left, but no dypnone. A little of fraction (5), collected separately when the b. p. was constant at 155°/9 mm. or 153°/8 mm. (Found: Br, 57·6. Calc. for $C_8H_6OBr_2$: Br, 57·6%), crystallised in ice–salt; it melted, however, at room temperature and therefore was not pure ωω-dibromoacetophenone. 20 G. of fraction (5) were redistilled and gave three fractions: (5L) 3·3 g., b. p. 100—124°/18 mm., (5I) 12·3 g., b. p. 134—156°/18 mm., (5U) 3·8 g., b. p. 156—168°/18 mm. and finally constant at 168°/18 mm. The separation by fractionation was very incomplete, since all the fractions contained acetophenone and ω-bromoacetophenone, as shown below.

Examination of the Fractions for Acetophenone.—A portion of the fraction was dissolved in methylated spirit (30 c.c.) and water (10 c.c.) containing semicarbazide hydrochloride (1·2 g.) and sodium acetate (1·2 g.) and maintained at 55° for 5 hours; water (200 c.c.) was then added:

Fraction	(1)	(2)	(3)	(4)	(5L)
Wt. taken (g.)	1·287	1·247	1·689	2·329	1·205
Wt. of crude semicarbazone (g.)	1·130	0·974	0·575	0·101	0·004

When the crude semicarbazones were separately recrystallised from methylated spirit, there was only slight loss in weight and the products had m. p.'s ranging from 190 to 195°. ω-Bromoacetophenone (1·5 g.), treated in exactly the same way as the fractions, gave a resinous solid (0·24 g.), m. p. 60—105° (ω-bromoacetophenone has m. p. 50°, and its semicarbazone has m. p. 146°; Knöpfer, *Monatsh.*, 1926, **119**, 145).

Examination of the Fractions for ω-Bromoacetophenone.—A portion of the fraction was dissolved in ethyl alcohol (50 c.c.) at 55°, succinic acid (1·5 g.) and sodium carbonate (1·1 g.) in water (5 c.c.) added, and the liquid maintained at 55° for 20 hours; the solid obtained was washed with water to remove sodium bromide:

Fraction	(1)	(2)	(3)	(4)	(5L)
Wt. taken (g.)	1·527	1·446	1·221	1·274	0·608
Wt. of succinate (g.)	0·006	0·010	0·074	0·081	0·006

The m. p. of the phenacyl succinate was 148° in every case. Fractions (3) and (4) were thus shown to contain much ω-bromoacetophenone.

ωω-Dibromoacetophenone, when similarly treated with sodium succinate, gave an oil but no crystalline solid. To show that phenacyl succinate could be prepared from ω-bromoacetophenone in presence of ωω-dibromoacetophenone and αβ-dibromostyrene, succinic acid (1·5 g.) and sodium carbonate (1·1 g.) in water (5 c.c.) were added to a hot solution of ω-bromoacetophenone (0·5 g.), ωω-dibromoacetophenone (2·8 g.), and αβ-dibromostyrene (5·4 g.) in ethyl alcohol (50 c.c.) and the whole was refluxed for 3 hours. The liquid was cooled and filtered, and the solid washed four times with ethyl alcohol (5 c.c.) and thrice with water (5 c.c.); the crystalline solid obtained (less than 0·1 g.) had m. p. 148° (Rather and Reid, *loc. cit.*, give m. p. 148°).

Examination of Fraction (5I) *for αβ-Dibromostyrene.*—Kinetic experiments showed that both mono- and di-bromoacetophenone suffered a rapid elimination of bromine at 25° on treatment with alcoholic potash, but that freshly prepared αβ-dibromostyrene suffered only a slow elimination. The method of separation therefore consisted in destruction of the first two compounds by alcoholic potash at room temperature and distillation of the low-boiling products from the higher-boiling αβ-dibromostyrene.

A solution of fraction (5I) in ethyl alcohol (100 c.c.) at room temperature was shaken for ½ minute with 2*N*-alcoholic potash (20 c.c.), 2*N*-hydrochloric acid (20 c.c.) promptly added, and the liquid immediately poured into water (1 l.) and extracted with ether. On distillation, two fractions were obtained, (*a*) 4·0 g., b. p. 95—134°/17 mm., (*b*) 5·0 g., b. p. 135—138°/17 mm., and some tar. Fraction (*b*) (Found: Br, 60·9. Calc. for $C_8H_6Br_2$: Br, 61·0%), like authentic αβ-dibromostyrene, became slightly cloudy and evolved hydrogen bromide on exposure to air for some time.

Examination of Fraction (5U) *for ωω-Dibromoacetophenone.*—A solution of fraction (5U) (3·8 g.) in methyl alcohol (75 c.c.) was mixed with hydroxylamine hydrochloride (6·0 g.) in

2*N*-sodium hydroxide (25 c.c.), and the acid liquid maintained at a moderate temperature for 6 hours, at room temperature for 24 hours, and then extracted with ether. Distillation of the ether from the extract left a white solid; this, crystallised from benzene, gave a solid (0·42 g.), m. p. 162° (Strassmann, *Ber.*, 1889, **22**, 419, gives m. p. 162° for "*anti*-phenyl*amphi*glyoxime"). Addition of ligroin to the benzene filtrate yielded a further 0·20 g. of impure solid, m. p. 150° (Schramm, *Ber.*, 1885, **18**, 353, gives m. p. 152° for the amorphous solid precipitated in this way). ω-Bromoacetophenone (1·0 g.), treated in an identical way, gave, on distillation of the ether, a thick oil which developed a surface film on cooling but from which no solid could be isolated. Hence this compound was not responsible for the formation of *anti*phenyl*amphi*glyoxime above.

Examination of Fraction (3) *for αα-Dibromoethylbenzene.*—This fraction became cloudy very quickly on exposure to air, whereas all the other original fractions remained clear. Bromine was displaced in dry alcohol alone. The time of displacement of half the replaceable bromine at 55° was 6·0 minutes, which agrees closely with the time of half-reaction of αα-dibromoethylbenzene in dry alcohol, namely, 6·2 minutes ($k_{\text{uni.}} = 0·112$ min.$^{-1}$). The procedure was to add 10 c.c. of the reaction mixture to 25 c.c. of benzene and 50 c.c. of water and titrate the liberated acid with *N*/10-sodium hydroxide. The weight of the fraction in dry ethyl alcohol (50 c.c.) was 1·6275 g., and the temperature 55°.

t	0	5·2	10·5	21·5	42·0	67·5
Titre	0·10	0·58	0·90	1·10	1·16	1·15

This would give a percentage of 4·3 of αα-dibromoethylbenzene in fraction (3). A much smaller proportion was found in (5L).

Preparation of ω-Bromoacetophenone from Phosphorus Chlorobromide and Acetophenone.—Phosphorus chlorobromide (160 g.) was added in small quantities with constant shaking to acetophenone (50 g.) cooled in ice-water; the temperature never exceeded 5°. After decomposition of the phosphorus compounds by ice-water the liquid was extracted with ether. Removal of the ether from the extract at room temperature left a thick pulp of crystals. By filtration and recrystallisation from ethyl alcohol a solid (27 g.) was obtained, m. p. and mixed m. p. with ω-bromoacetophenone 50° (Found : Br, 40·4. Calc. : Br, 40·2%), oxidation of which with alkaline permanganate yielded benzoic acid (m. p. and mixed m. p.). The filtrate (20 g.) gave three fractions on distillation : (1) 3·5 g. (semicarbazone, m. p. 195°), b. p. 80—131°/15 mm. (Found : Br, 16·4%); (2) 10·5 g., b. p. 131—136°/15 mm. (Found : Br, 44·3%), contained ω-bromoacetophenone, b. p. 134°/15 mm., m. p. and mixed m. p. 50°; (3) 3·0 g., b. p. 136—145°/15 mm. (Found : Br, 54·3%), probably a mixture of mono- and di-bromoacetophenones and αβ-dibromostyrene.

Action of Phosphorus Chlorobromide on ω-Bromoacetophenone.—Phosphorus chlorobromide (32 g., *i.e.*, a large excess) was added all at once to ω-bromoacetophenone (7 g.) and the temperature was maintained at 20° for 15 minutes; there was a vigorous evolution of hydrogen bromide. The temperature was raised to 55° for 5 minutes, and the liquid then left at room temperature for 2 hours. After the usual water–ether treatment a liquid (7·0 g.), b. p. 131—146°/10 mm. (Found : Br, 58·7%), was obtained. On redistillation two fractions were separated : (1) 2·8 g., b. p. 130—137°/8 mm. (Found: Br, 59·5%); (2) 4·0 g., b. p. 138—142°/7 mm. (Found: Br, 57·5. Calc. for $C_8H_6OBr_2$: Br, 57·6%). Fraction (1) was probably mainly αβ-dibromostyrene (Calc. : Br, 61·0%) with some dibromoacetophenone. Fraction (2), cooled in ice–salt, gave crystals, m. p. 35—36° alone or mixed with authentic ωω-dibromoacetophenone.

Action of Phosphorus Pentachloride on Acetophenone.—Experiment I. Acetophenone (60 g.) was added to phosphorus pentachloride (105 g.) at 15°. The temperature rose to 75° in 10 minutes, a vigorous evolution of hydrogen chloride taking place, and then fell to 50°, the evolution becoming slow; the reaction was apparently completed in 20 minutes at 70°. After the usual water–ether treatment, distillation gave four fractions : (1) 27·5 g., b. p. 80—86°/17 mm. (Found : Cl, 15·9%); (2) 22·2 g., b. p. 86—88°/17 mm. (Found : Cl, 16·0%); (3) 4·0 g., b. p. 88—90°/18 mm. (Found : Cl, 16·0%); (4) 3·0 g., b. p. 90—105°/20 mm. (Found : Cl, 12·2%). There was some residual tar. All the fractions fumed, but were not lachrymatory; they were examined for acetophenone as in the chlorobromide experiments (p. 306) :

Fraction	(1)	(2)	(3)	(4)
Wt. taken (g.)	1·131	1·343	0·361	0·708
Wt. of crude semicarbazone (g.)	0·560	0·970	0·659	0·475

Recrystallisation of the crude semicarbazone from methylated spirit had a result similar to that in the chlorobromide experiments. From the b. p.'s (cf. ω-chloroacetophenone, b. p. 244°), chlorine contents, and weights of semicarbazone, it appeared that the fractions contained α-chlorostyrene. In an attempt to isolate α-chlorostyrene, after filtration of the semicarbazone from fraction (1), an oil (0·3 g.) was obtained which had Cl, 15·2%. The separation therefore was not satisfactory. Fraction (4) was examined for αα-dichloroethylbenzene in a manner similar to that for αα-dibromoethylbenzene (p. 307) at 55°; the weight of the fraction in dry ethyl alcohol (50 c.c.) was 1·0900 g.:

t	0	34	105	343	1380
Titre	0·90	1·20	1·60	1·90	1·90

From these figures the time of displacement of half the replaceable chlorine was 64 minutes, which approximates to the time of half-reaction of αα-dichloroethylbenzene in dry ethyl alcohol, namely, 53 minutes ($k_{\text{uni.}} = 0{\cdot}0131$ min.$^{-1}$). This compound therefore was probably present to the extent of 4% in fraction (4).

Experiment II. Phosphorus pentachloride (40 g.) was added with shaking to acetophenone (20 g.), cooled in ice-water, during 10 minutes. There was little or no evolution of hydrogen chloride and the liquid was left overnight at room temperature. After the usual water–ether treatment, three fractions were obtained: (1) 19 g., b. p. 79—82°/10 mm. (Found: Cl, 9·6%); (2) 3 g., b. p. 82—110°/10 mm. (Found: Cl, 5·9%); (3) 4 g., b. p. 203—204°/10 mm. (Found: Cl, 0). Fractions (1) and (2) contained acetophenone, and probably some α-chlorostyrene; 5 g. of (1) yielded 5 g. of acetophenonesemicarbazone, and 3 g. of (2) gave 3·4 g. of this semicarbazone. (3) was dypnone (Found: C, 86·6; H, 6·7. Calc. for $C_{16}H_{14}O$: C, 86·5; H, 6·3%).

Action of Phosphorus Pentabromide on Acetophenone.—Phosphorus pentabromide (95 g.) was added during 1 hour to acetophenone (26 g.); the temperature was mainly 15° and never exceeded 17° and the evolution of hydrogen bromide could be stopped immediately by immersion of the reaction flask in ice-water. The liquid was left at room temperature for 2 hours. After the usual water–ether treatment two fractions were obtained, both being dark brown, viscous, fuming liquids: (1) 2·6 g., b. p. 50—80°/30 mm. (Found: Br, 34·6%); (2) 5·1 g., b. p. 80—95°/21 mm. (Found: Br, 26·1%). The main product, however, was a non-volatile thick tar, from which chloroform extracted nothing that could be crystallised. Fractions (1) and (2), examined for ω-bromoacetophenone, gave the following yields of phenacyl succinate:

Fraction	(1)	(2)
Wt. taken (g.)	0·763	1·942
Wt. of succinate (g.)	0·005	0·015

Traces of sodium bromide were present in both specimens of succinate. Examination for acetophenone as before showed that the fractions mainly consisted of this compound:

Fraction	(1)	(2)
Wt. taken (g.)	0·761	1·493
Wt. of crude semicarbazone (g.)	0·212	1·063

Summary.

1. The action of a phosphorus pentahalide (PCl_5, PCl_3Br_2, PBr_5) on acetophenone yields a variety of products.

2. The formation of these products is probably due to the existence of the keto-enol equilibrium system (acetophenone) and the thermal equilibrium system of the phosphorus halide.

3. By assuming (*a*) that halogen substitution for carbonyl oxygen or for hydroxyl proceeds by the action of the phosphorus halide, and (*b*) that halogen addition occurs owing to the presence of free halogen, the results can be interpreted.

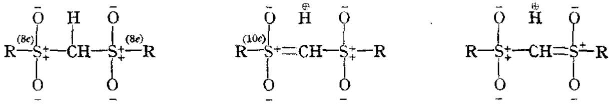
The Polytechnic, Regent Street, London, W. 1. [*Received, December 1st, 1936.*]

64. *Influence of Poles and Polar Linkings on Tautomerism in the Simple Three-carbon System. Part IV. Activation by Sulphonyl Groups.*

By Eugene Rothstein.

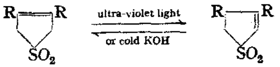
When a methylene group is activated by a sulphonyl radical $-\overset{++}{S}O_2R$, its reactivity is in many respects comparable with that in a β-diketone. The greater part of the activation, however, arises from the two positive charges on the sulphur atom, which promote the loosening of the C–H bond of the methylene group in contradistinction to the diketones, where enolisation is the main factor (compare Arndt and Martius, *Annalen*, 1932, **499**, 228; *Ann. Reports*, 1934, 193). There have, in recent years, been several suggestions that the sulphur atom may in certain cases expand its valency shell (Ingold and Jessop, J., 1930, 708; Kohler and Larson, *J. Amer. Chem. Soc.*, 1935, **57**, 1448; Connor, Fleming, and Clayton, *ibid.*, 1936, **58**, 1386), and there are other cases where an expansion of the sulphur octet is indicated. Both bis(ethylsulphonyl)phenylthiomethane, $(Et{\cdot}SO_2)_2CH{\cdot}SPh$ (Laves, *Ber.*, 1890, **23**, 1414), and bis(phenylsulphonyl)phenylthiomethane (Fromm, *Annalen*, 1889, **253**, 1386) are sufficiently strong acids to decompose warm sodium carbonate solution, the corresponding bissulphonylmethanes being soluble in alkali hydroxide only (Shriner, Struck, and Jorison, *J. Amer. Chem. Soc.*, 1930, **52**, 2060).

It is suggested that in addition to the $-I$ effect of the sulphonyl group, there is a mesomeric effect arising from the resonance between the canonical structures:



This must be interpreted, not that the hydrogen atom is for any appreciable moment of time actually ionised, but that the electron pair of the C–H bond tends to be distributed over the whole system. Since the contributions of the wave functions of the second and third canonical structures are probably small, the actual effect will be a loosening of the proton involved, with a consequent localisation of a small negative charge on some other part of the system. Although small, the effect appears appreciable. For instance, whereas a bissulphonylmethane, $(R{\cdot}SO_2)_2CH_2$, will dissolve in sodium hydroxide solution but will not react with diazomethane, trimethylenetrisulphone, $CH_2{<}{}^{SO_2-CH_2}_{SO_2-CH_2}{>}SO_2$, is methylated (Arndt and Martius, *loc. cit.*), and similarly, whilst bis(phenylsulphinyl)methane, $(Ph{\cdot}SO)_2CH_2$, will only react with alkali hydroxide in alcoholic solution, trimethylenetrisulphoxide, $CH_2{<}{}^{SO-CH_2}_{SO-CH_2}{>}SO$, easily dissolves in 10% sodium hydroxide solution to give the sodio-derivative (Hinsberg, *J. pr. Chem.*, 1912, **85**, 337), the extra resonance in the ring system leading to a greater fractional ionisation of the hydrogen atom.

This view receives confirmation from the interconvertibility of the cyclic butadienes and their derivatives (Böeseken and van Zuydewijn, *Proc. K. Akad. Wentsch. Amsterdam*, 1934, **37**, 760; 1936, **39**, 31; *Rec. trav. chim.*, 1934, **53**, 673; Backer and Strating, *ibid.*, 1935, **54**, 618):



On the other hand it was shown in Part III (Rothstein, J., 1934, 684) that benzyl-Δ^{α}- and -Δ^{β}-propenylsulphones, $CH_2Ph{\cdot}SO_2{\cdot}CH{:}CH{\cdot}CH_3$ and $CH_2Ph{\cdot}SO_2{\cdot}CH_2{\cdot}CH{:}CH_2$, are not tautomeric.

It follows, therefore, that a three-carbon unsaturated system terminated by sulphonyl

groups should be considerably more mobile than the corresponding bis-ammonium salts (Ingold and Rothstein, J., 1931, 1666), because in addition to the enhanced polar effect of the sulphonyl radicals, resonance between the following canonical structures (not possible with the ammonium salts) is to be expected:

$$R{-}SO_2{-}\overset{H}{C}H{-}CH{=}CH{-}SO_2R \qquad R{-}SO_2{=}\overset{H}{C}H{-}CH{=}CH{-}SO_2R$$

$$R{-}SO_2{-}\overset{H}{C}H{=}CH{-}CH{=}SO_2R \qquad R{-}SO_2{-}\overset{H}{C}H{=}CH{-}\bar{C}H{-}\overset{++}{S}O_2R$$

α-Benzylsulphonyl-γ-ethylsulphonyl-Δ^{α}- and -Δ^{β}-propene (I and II) have accordingly been synthesised by various methods,

$$\underset{\text{(I.)}}{CH_2Ph{\cdot}SO_2{\cdot}CH{:}CH{\cdot}CH_2{\cdot}SO_2Et} \rightleftharpoons \underset{\text{(II.)}}{CH_2Ph{\cdot}SO_2{\cdot}CH_2{\cdot}CH{:}CH{\cdot}SO_2Et}$$

which, however, always lead to a mixture of the two isomerides. By careful fractional crystallisation small quantities of each could be obtained, the Δ^{β}-sulphone (II) being quite pure, and the other probably containing a small amount of its isomeride. The two sulphones differed in appearance, solubility, and melting point, a mixture of the two showing a depression. Interconversion was exceedingly facile, being rapid in solvents such as methyl alcohol, and rather slower in ethyl acetate or benzene, and also taking place to some extent when the substance was heated above its melting point. It was for this reason that (I), which has the greater solubility and apparently the lower melting point, cannot be obtained quite free from (II), since repeated crystallisations lead to interconversion. The equilibrium mixture contained 40% of the Δ^{β}-sulphone, this figure representing a lower limit for this isomeride.

The structure of the sulphones was shown by their reduction with hydrogen in the presence of Adams's catalyst to *α-benzylsulphonyl-γ-ethylsulphonylpropane*, the product being identified by analysis and by comparison with the synthetic bis-sulphone prepared from trimethylene chlorohydrin. Furthermore, fission by ozone showed that the two sulphones were not stereoisomerides, since the corresponding sulphonylacetic acids were isolated (among other products), whereas pure (II) gave *benzylsulphonylacetic acid* only, no ethylsulphonylacetic acid being detected:

$$R{\cdot}SO_2{\cdot}CH_2{\cdot}CH{:}CH{\cdot}SO_2R' \longrightarrow \underset{\text{(III, R = benzyl or ethyl.)}}{R{\cdot}SO_2{\cdot}CH_2{\cdot}CO_2H} + R'{\cdot}SO_3H + HCHO$$

The proportions of these acids were determined by their conversion into the corresponding sulphones, $R{\cdot}SO_2{\cdot}CH_3$, which were then submitted to thermal analysis. The above fission did not prove a suitable method for estimating the percentage of each isomeride in the original mixture of the sulphones, since among the products obtained were the unchanged sulphones, the corresponding aldehydes and sulphonic acids, together with small quantities of formaldehyde and formic acid. A melting-point curve was therefore constructed from artificial mixtures of the two isomerides and used for this determination. The figures roughly corresponded to those obtained by ozonolysis.

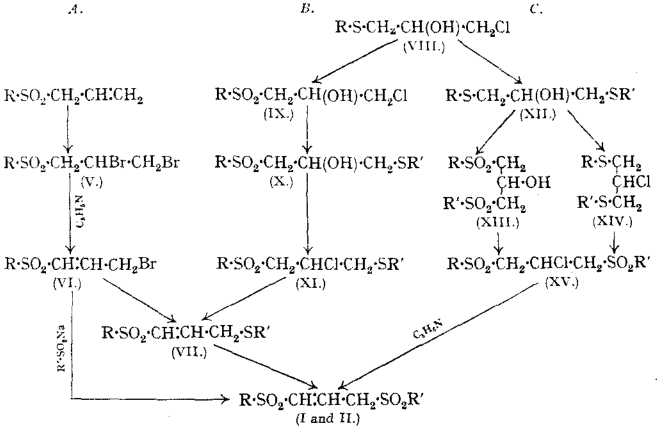
It has been postulated that there are a larger number of wave functions contributing to the mesomeric state of the propene systems than in the case of the bissulphonylmethanes. Consequently an enhanced reactivity might be expected in the former case. Definite evidence of this is provided by the condensation with benzaldehyde in the presence of piperidine with the production of *(βδ)-benzylsulphonylethylsulphonyl-α-phenylbutadiene* (IV) (the orientation of the ethyl and benzyl groups not yet having been determined owing to the experimental difficulties encountered); the same condensation product is obtained starting with either of the isomerides:

$$\text{(I) or (II)} + Ph{\cdot}CHO \longrightarrow \underset{\text{(IV, R and R' = benzyl or ethyl.)}}{R{\cdot}SO_2{\cdot}CH{:}CH{\cdot}C(SO_2R'){:}CHPh}$$

Likewise, there is also a reaction with diazomethane (following paper). Bis(phenyl-

sulphonyl)methane will not condense with benzaldehyde or other reagents diagnostic of an active methylene group (Connor, Fleming, and Clayton, *loc. cit.*).

The methods used for the preparation of the bissulphonylpropenes are summarised in the following diagram. As in any case each of them led to the formation of both isomerides, route B was adopted as the most convenient when further quantities were required, since the product at each stage of the synthesis could be obtained relatively pure. It may be noted that *α-benzylsulphonyl-γ-ethylthio-Δ^α-propene* (VII, R = benzyl, R′ = ethyl) should have had the structure indicated when prepared from VI (R = benzyl), but fission with ozone yielded products which showed that a considerable proportion of the Δ^{β}-isomeride was present. Since it is possible that oxidation to the bis-sulphone preceded fission, this is not regarded as conclusive evidence that the presence of a terminal thio-group enhances the mobility of the system.



(R and R′ = benzyl or ethyl.)

Experimental.

(A) *Preparation of α-Benzyl-γ-ethyl-Δ^α- and -Δ^β-propenes.—Route A.**—Benzyl-Δ^{β}-propenylsulphone, prepared from benzylthiol-Δ^{β}-propene (v. Braun and Engelbertz, *Ber.*, 1923, **56**, 1573) by oxidation with perhydrol, had b. p. 198°/12 mm., and was identical (m. p. and mixed m. p.) with that obtained from sodium benzylsulphinate and allyl bromide (Part III, *loc. cit.*). It was dissolved in chloroform, and the theoretical quantity of bromine in carbon tetrachloride solution slowly added. Heat was developed, and the evolution of a small amount of hydrogen bromide indicated that substitution was taking place. Distillation of the solvent yielded *βγ-dibromo-α-benzylsulphonylpropane* (V, R = CH_2Ph), which crystallised from benzene–petrol in prisms, m. p. 85—87°; yield, 70% (Found: C, 33·7; H, 3·6; Br, 44·5. $C_{10}H_{12}O_2Br_2S$ requires C, 33·7; H, 3·4; Br, 44·9%).

γ-Bromo-α-benzylsulphonyl-Δ^α-propene (VI, R = benzyl). The dibromo-sulphone (10 g.) was heated under reflux on the steam-bath for 1 hour with pyridine (2·2 g.) and benzene (40 c.c.). The benzene solution, after being washed with dilute hydrochloric acid and dried, yielded a crystalline solid, which separated from benzene–petrol (b. p. 40—60°) in short needles, m. p.

* The alternative paths of both route A and B were followed in the expectation of synthesising the Δ^{α}- and Δ^{β}-bissulphones separately. Partly owing to the highly mobile nature of these compounds, this expectation was not realised.

95—97°; yield, 52% (Found: C, 43·4; H, 3·9; Br, 29·1. $C_{10}H_{11}O_2BrS$ requires C, 43·6; H, 4·0; Br, 29·1%). The mother-liquor contained a mixture consisting mainly of unchanged dibromide. The monobromide depressed the m. p. of the initial material and of *γ-bromo-α-benzylsulphonyl-Δ^β-propene*, m. p. 151—152° (long needles from ethyl alcohol or ethyl acetate), prepared from αγ-dibromopropene and sodium benzylsulphinate (Found: C, 44·1; H, 4·0; Br, 29·0. $C_{10}H_{11}O_2BrS$ requires C, 43·6; H, 4·0; Br, 29·1%). Unlike the Δ^{α}-isomeride, it did not condense with sodium ethylthiol or sodium benzylsulphinate. The terminal position of the bromine atom in the Δ^{α}-compound was shown by the structure of the subsequent condensation products.

The pyridine liquors contained about 40% of the dibromo-compound originally taken. On basification a pale yellow solid was liberated, but its constitution has not yet been determined owing to the rapidity with which it polymerised.

βγ-Dichloro-α-benzylsulphonylpropane was obtained in poor yield by passing chlorine through a chloroform solution of benzylsulphonyl-Δ^{β}-propene, and crystallising the product from either ether or benzene–petrol (b. p. 40—60°); m. p. 65°, b. p. 215—220°/3 mm. It was identical (m. p. and mixed m. p.) with the product of the reaction between γ-chloro-β-hydroxy-α-benzylsulphonylpropane (IX, R = benzyl) and phosphorus pentachloride (Found: C, 45·2; H, 4·8; Cl, 26·3. $C_{10}H_{12}O_2Cl_2S$ requires C, 44·9; H, 4·5; Cl, 26·6%).

γ-Chloro-α-benzylsulphonyl-Δ^{α}-propene, obtained from the dichloro-sulphone by boiling it with pyridine in benzene solution, crystallised from benzene–petrol in feathery clusters of needles, m. p. 75—76° (Found: C, 52·2; H, 4·8; Cl, 15·3. $C_{10}H_{11}O_2ClS$ requires C, 52·0; H, 4·8; Cl, 15·4%).

Condensation of γ-Bromo-α-benzylsulphonyl-Δ^{α}-propene with sodium ethylthiol. α-Benzylsulphonyl-γ-ethylthiopropene (VII, R = benzyl, R′ = ethyl), b. p. 190—196°/0·2 mm., was obtained by addition of the bromo-sulphone in alcoholic solution to sodium ethylthiol (10% excess) cooled in ice. It evidently contained benzylsulphonylbis(ethylthio)propane (cf. below), which accounts for the faulty analysis (Found: C, 55·5; H, 6·9; S, 26·4. $C_{12}H_{16}O_2S_2$ requires C, 56·3; H, 6·3; S, 25·0%). It was obtained pure by method B.

α-Benzylsulphonyl-γ-ethylsulphonyl-Δ^{α}- and -Δ^{β}-propene (I and II). Oxidation of the above thiosulphone with perhydrol yielded a white semi-solid, which after rubbing with methyl alcohol crystallised from the same solvent in platelets, m. p. 129—130°. This was the Δ^{β}-isomeride (section C). The mother-liquors contained a mixture of the two sulphones (Found: C, 49·8; H, 6·1; S, 22·5. $C_{12}H_{16}O_4S_2$ requires C, 50·0; H, 5·6; S, 22·2%).

α-Benzylsulphonyl-βγ(?)-bis(ethylsulphonyl)propane, $CH_2Ph\cdot SO_2\cdot CH_2\cdot CH(SO_2Et)\cdot CH_2\cdot SO_2Et$, was furnished by the cold methyl-alcoholic filtrate (above); it separated from methyl alcohol in needles, m. p. 119—120°, depressed by the above bis-sulphone (Found: C, 43·9; H, 5·9; S, 25·4; *M*, 394, 389. $C_{14}H_{22}O_6S_3$ requires C, 44·0; H, 5·8; S, 25·1%; *M*, 382).

The bis-sulphone (together with the tris-sulphone) was also obtained in 78% yield by boiling an alcoholic solution of the bromo-compound with an excess of sodium benzylsulphinate (Found: C, 49·7; H, 5·7%; *M*, 328. $C_{12}H_{16}O_4S_2$ requires *M*, 288).

α-Ethylsulphonyl-Δ^{β}-propene, $Et\cdot SO_2\cdot CH_2\cdot CH{:}CH_2$, prepared by the oxidation of the corresponding sulphide (Dawson, *J. Amer. Chem. Soc.*, 1933, **55**, 2070) with perhydrol in glacial acetic acid solution, had b. p. 129°/11 mm.; yield, 72% (Found: C, 44·7; H, 7·7; S, 23·9. $C_5H_{10}O_2S$ requires C, 44·8; H, 7·4; S, 23·9%).

βγ-Dibromo-α-ethylsulphonylpropane (V, R = ethyl). Bromine (24 g.) in carbon tetrachloride (120 c.c.) was slowly added to a cooled solution of α-ethylsulphonyl-Δ^{β}-propene (20 g.) in chloroform (100 c.c.). After removal of the solvent, the residue was distilled, b. p. 166°/0·6 mm.; yield, 95% (Found: C, 20·8; H, 3·8; Br, 53·6. $C_5H_{10}O_2Br_2S$ requires C, 20·4; H, 3·4; Br, 54·5%).

Action of Pyridine on βγ-Dibromo-α-ethylsulphonylpropane.—Boiling the dibromide with pyridine yielded mixtures of the monobromide with the dibromide. The yield of sulphone was smaller when excess of pyridine was used, but there was little change in the composition of the mixture. In a typical case (yield of sulphones, 55%), distillation gave three fractions, the lowest having b. p. 164°/0·7 mm. (Found: C, 25·2; H, 4·3; Br, 44·2%), and the highest b. p. 171°/0·7 mm. (Found: C, 21·3; H, 3·3; Br, 52·0. $C_5H_7O_2BrS$ requires C, 28·1; H, 4·2; Br, 36·1%), *i.e.*, there was very little separation, and the lower b. p. fraction contained 40—50% of dibromide.

Nevertheless, when an alcoholic solution of the lower fraction was boiled under reflux with twice its weight of sodium benzylsulphinate, an 85% yield of the bis-sulphone (I and II) was obtained. It contained a large proportion of (II), since it had m. p. 127—129° after two recrys-

tallisations from methyl alcohol (Found : C, 49·9; H, 5·5%). No trace of tris-sulphone was detected.

Route B.—*γ-Chloro-β-hydroxy-α-benzylthiopropane* (VIII, R = benzyl). Sodium benzylthiol (from 80 g. of benzylthiol), dissolved in ethyl alcohol (200 c.c.), was slowly added to a well-cooled and stirred solution of αγ-dichlorohydrin (200 g.) in ethyl alcohol (200 c.c.). After 1 hour, the mixture was diluted with water (500 c.c.) and extracted with ether. The *chloro-sulphide*, b. p. 123°/0·05 mm. (yield, 72%), usually contained as an impurity benzyl sulphide, which could not be entirely removed by fractional distillation. This accounts for the rather low chlorine content (Found : C, 55·8; H, 6·5; Cl, 14·3. $C_{10}H_{13}OClS$ requires C, 55·4; H, 6·0; Cl, 16·4%).

γ-Chloro-β-hydroxy-α-benzylsulphonylpropane (IX, R = benzyl). The chloro-sulphide was warmed on the steam-bath for 45 minutes, in portions not greater than 25 g. at a time, with perhydrol in glacial acetic acid. The precipitate obtained when the liquid was added to excess of water was crystallised from ethyl alcohol, yielding dibenzylsulphone, m. p. and mixed m. p. 150° (Found : C, 68·4; H, 5·5; S, 13·0. Calc. : C, 68·3; H, 5·7; S, 13·0%). The alcoholic filtrate was evaporated to dryness, and the residue again crystallised from alcohol, this process being repeated until no more dibenzylsulphone separated. Finally, the residue was crystallised from benzene, the *chlorosulphone* separating in needles, m. p. 97—98°; yield, 70% (Found : C, 48·2; H, 5·4; Cl, 13·7; S, 13·1. $C_{10}H_{13}O_3ClS$ requires C, 48·3; H, 5·2; Cl, 14·3; S, 12·9%).

β-Hydroxy-γ-ethylthio-α-benzylsulphonylpropane (X, R = benzyl, R′ = ethyl). The chloro-sulphone (66 g.), dissolved in methyl alcohol (400 c.c.), was added to a slight excess of sodium ethylthiol in the same solvent. After 12 hours, the liquid was boiled for ½ hour under reflux. The resulting *sulphide-sulphone* was extracted from the diluted solution with chloroform and had b. p. 225°/0·5 mm. (slight decomp.); yield, 90% (Found : C, 52·4; H, 6·6; S, 23·1. $C_{12}H_{18}O_3S_2$ requires C, 52·6; H, 6·6; S, 23·4%).

β-Chloro-γ-ethylthio-α-benzylsulphonylpropane (XI, R = benzyl, R′ = ethyl) was prepared by the cautious addition of phosphorus pentachloride (30 g.) to a hot solution of the hydroxy-compound (33 g.) in chloroform (150 c.c.), the product being then boiled under reflux for 10 minutes. The solvent was removed in a vacuum at the ordinary temperature, since the residue became black when heated and did not subsequently solidify. It crystallised from benzene-petrol (b. p. 40—60°) in long feathery needles, m. p. 56—58°, soluble in ether, alcohol and benzene; yield, about 95% (Found : C, 49·4; H, 5·8; Cl, 11·9; S, 21·8. $C_{12}H_{17}O_2ClS_2$ requires C, 49·2; H, 5·8; Cl, 12·1; S, 21·9%).

α-Benzylsulphonyl-γ-ethylthiopropene (VII, R = benzyl, R′ = ethyl). The chloro-sulphone (XI) (40 g.) was boiled under reflux for 2 hours with pyridine (150 c.c.), and the resulting liquid extracted with chloroform after dilution and acidification. The residue obtained after removal of the solvent was distilled in portions of not more than 10 c.c. at a time in order to avoid the decomposition which otherwise usually occurred; b. p. 176°/0·02 mm.; yield, 82% (Found : C, 56·6; H, 6·2; S, 24·6. $C_{12}H_{16}O_2S_2$ requires C, 56·3; H, 6·3; S, 25·0%). Oxidation of (VII) with perhydrol gave the usual mixture of (I) and (II) (Found : C, 50·1; H, 5·6%; *M*, 299).

γ-Chloro-β-hydroxy-α-ethylthiopropane (VIII, R = ethyl). Sodium ethylthiol (from 50 g. of ethylthiol), dissolved in 66% aqueous ethyl alcohol (150 c.c.), was slowly added to a cold stirred solution of αγ-dichlorohydrin (200 g.) in the same solvent (200 c.c.), and boiled for 10 minutes. After dilution with water, the *sulphide* was extracted with ether and dried with potassium carbonate. Removal of the solvent left an oil, b. p. 100°/9 mm.; yield, 66% (Found : C, 38·6; H, 7·1; Cl, 23·4. $C_5H_{11}OClS$ requires C, 38·8; H, 7·1; Cl, 23·0%). Unless the fractionation was very carefully carried out, a small amount of dichlorohydrin was subsequently found in the sulphide.

γ-Chloro-β-hydroxy-α-ethylsulphonylpropane (IX, R = ethyl). The chloro-sulphide (VIII) (20 g.) was gently warmed with perhydrol (38 c.c.) in glacial acetic acid (100 c.c.) for ¾ hours, water-cooling being used when the reaction became vigorous. The resulting *sulphone* was too soluble in water to be extracted by chloroform or ether, and the liquid was therefore fractionated in a vacuum. The residual oil had b. p. 141°/0·1 mm. (yield, 84%), crystallised on standing, and separated from ether in needles, m. p. 49° (Found : C, 32·4; H, 6·0; Cl, 18·9; S, 16·9. $C_5H_{11}O_3ClS$ requires C, 32·2; H, 5·9; Cl, 19·0; S, 17·2%).

β-Hydroxy-γ-benzylthio-α-ethylsulphonylpropane (X, R = ethyl, R′ = benzyl), obtained in 90% yield by the addition of the chloro-sulphone (IX) (32 g.), dissolved in alcohol (50 c.c.), to sodium benzylthiol (from 25 g. of benzylthiol) in 80% aqueous alcohol (120 c.c.), had b. p. 216°/0·3 mm. (Found : C, 52·7; H, 6·9; S, 23·2. $C_{12}H_{18}O_3S_2$ requires C, 52·6; H, 6·6; S, 23·4%).

Action of phosphorus pentachloride on (X). A hot solution of the hydroxy-sulphide-sulphone (44 g.) in chloroform (100 c.c.) was slowly treated with phosphorus pentachloride (36 g.). The dark brown residue after distillation of the solvent could not be satisfactorily purified, as it did not solidify, and distillation was attended by decomposition (b. p. 220°/1·3 mm.). It was therefore boiled for 2 hours with pyridine (40 c.c.), and the diluted solution acidified and extracted with chloroform, whence *γ-benzylthio-α-ethylsulphonyl-Δ$^{\alpha}$-propene* (VII, R = ethyl, R′ = benzyl) was obtained as a rather cloudy, pale yellow liquid, b. p. 171°/0·02 mm.; yield, 60% (Found: C, 56·9; H, 6·1; S, 24·8. $C_{12}H_{16}O_2S_2$ requires C, 56·3; H, 6·3; S, 25·0%). Oxidation with perhydrol yielded the bis-sulphones (I and II) (Found: C, 49·7; H, 5·7; S, 22·1%).

Route C.—*β-Hydroxy-α-benzylthio-γ-ethylthiopropane* (XII, R, R′ = benzyl, ethyl) was prepared by the addition of γ-chloro-β-hydroxy-α-ethylthiopropane (76 g.) to sodium benzylthiol (from 70 g. of benzylthiol) in 75% alcohol (200 c.c.); b. p. 162—163°/0·2 mm.; yield, 86% (Found: C, 58·9; H, 7·6; S, 27·0. $C_{12}H_{18}OS_2$ requires C, 59·5; H, 7·4; S, 26·4%). Owing to the presence of some unchanged dichlorohydrin in the chloro-sulphone, a fraction, b. p. 215°/0·2 mm., was obtained. This was mainly *β-hydroxy-αγ-bis(benzylthio)propane* (Found: C, 65·0; H, 6·7; S, 22·2. $C_{17}H_{20}OS_2$ requires C, 67·1; H, 6·6; S, 21·5%), since oxidation with perhydrol yielded the corresponding *β-hydroxy-αγ-bis(benzylsulphonyl)propane*, which crystallised from glacial acetic acid in small plates, m. p. 204—205° (Found: C, 55·3; H, 5·4; S, 17·6. $C_{17}H_{20}O_5S_2$ requires C, 55·4; H, 5·4; S, 17·4%). It was insoluble in ethyl acetate, acetone, alcohol and chloroform.

β-Hydroxy-α-benzylsulphonyl-γ-ethylsulphonylpropane (XIII), obtained by the oxidation of (XII) with perhydrol, separated from ethyl acetate in needles, m. p. 143—144°. It did not condense with benzaldehyde in the presence of piperidine (Found: C, 47·4; H, 6·3; S, 21·0. $C_{12}H_{18}O_5S_2$ requires C, 47·1; H, 5·9; S, 20·9%).

β-Chloro-α-benzylthio-γ-ethylthiopropane (XIV). The hydroxy-bis-sulphide (XII) (16 g.) was warmed under reflux with thionyl chloride (6 c.c.) in benzene (10 c.c.). Fractional distillation gave the *chloro-sulphide*, b. p. 144—145°/0·2 mm., in 88% yield (Found: C, 56·0; H, 7·2; S, 24·4. $C_{12}H_{17}ClS_2$ requires C, 55·3; H, 6·5; S, 24·6%). It was stable to boiling pyridine.

β-Chloro-α-benzylsulphonyl-γ-ethylsulphonylpropane (XV). The chloro-bis-sulphide (45 g.) was cautiously oxidised by perhydrol (100 c.c.) in glacial acetic acid (300 c.c.), water-cooling being employed when the reaction became vigorous. The resulting *sulphone*, which contained a considerable amount of unidentified by-product, crystallised from ethyl alcohol in platelets, m. p. 105—107°; yield, 48% (Found: C, 44·6; H, 5·5; Cl, 10·8; S, 18·9. $C_{12}H_{17}O_4ClS_2$ requires C, 44·4; H, 5·2; Cl, 10·9; S, 19·7%). It was also obtained by the action of phosphorus pentachloride (12 g.) on the hydroxy-bis-sulphone (12 g.) dissolved in chloroform (100 c.c.). The hydrogen chloride was eliminated in the usual way by boiling pyridine to yield the bis-sulphones (I) and (II).

(B) (i) *Preparation of α-Benzylsulphonyl-γ-ethylsulphonylpropane.*—*γ-Hydroxy-α-ethylthiopropane*, SEt·CH_2·CH_2·CH_2·OH, b. p. 104°/15 mm., was prepared in 76% yield from trimethylene chlorohydrin (35 g.) and sodium ethylthiol (from 25 g. of ethylthiol) (Found: C, 49·8; H, 10·3; S, 26·4. $C_5H_{12}OS$ requires C, 50·0; H, 10·0; S, 26·7%). The corresponding chloro-sulphide was obtained in 64% yield by boiling under reflux a mixture of the hydroxy-sulphide (20 g.), dissolved in benzene (10 c.c.), with thionyl chloride (15 c.c.); b. p. 73°/14 mm.

γ-Benzylthio-α-ethylthiopropane, SEt·CH_2·CH_2·CH_2·S·CH_2Ph, prepared from the chloro-sulphide and sodium benzylthiol, had b. p. 135°/0·3 mm.; yield, 88% (Found: C, 63·1; H, 7·8; S, 28·0. $C_{12}H_{18}S_2$ requires C, 63·7; H, 8·0; S, 28·3%). Oxidation with perhydrol gave *γ-benzylsulphonyl-α-ethylsulphonylpropane* in 91% yield. It crystallised from ethyl acetate in needles, m. p. 153—154° (Found: C, 49·6; H, 6·4; S, 22·2. $C_{12}H_{18}O_4S_2$ requires C, 49·7; H, 6·2; S, 22·1%). It did not react with alkali alkoxide, and no condensation product was formed when it was mixed with benzaldehyde and piperidine.

(ii) *Preparation of ethylsulphonylacetic acid* (III, R = ethyl). Ethyl ethylthioacetate was prepared from ethyl chloroacetate and sodium ethylthiol (Klason, *Bull. Soc. chim.*, 1875, **23**, 444); b. p. 65°/9 mm. (Found: C, 48·7; H, 8·2. Calc.: C, 48·6; H, 8·1%). Oxidation with perhydrol gave the corresponding sulphone, b. p. 110°/0·3 mm. (not previously recorded) (Found: C, 40·2; H, 6·7; S, 17·9. Calc.: C, 40·0; H, 6·7; S, 17·8%). Hydrolysis was best accomplished by warming the ester with concentrated hydrochloric acid and evaporating the resulting solution to dryness. A nearly theoretical yield of the acid was obtained, and it solidified when kept in a desiccator for some time, having m. p. 62—64°. It has not previously been isolated in crystalline form (Found: C, 31·5; H, 5·5; S, 20·6. Calc.: C, 31·6; H, 5·3; S, 21·1%). The

acid lost carbon dioxide when heated, decomposition commencing at 210° and being complete at 240—250°. The yield of methylethylsulphone was over 84%, this being a minimum figure owing to the difficulty of keeping the original acid completely water-free.

(iii) *Preparation of benzylsulphonylacetic acid* (III, R = benzyl). Ethyl benzylthioacetate (Johnson and Guest, *Amer. Chem. J.*, 1909, **42**, 278), b. p. 129°/0·7 mm., was oxidised with perhydrol to give *ethyl benzylsulphonylacetate*, which crystallised from benzene–petrol (b. p. 40—60°) in needles, m. p. 50°; yield, 88% (Found: C, 54·7; H, 5·8; S, 13·2. $C_{11}H_{14}O_4S$ requires C, 54·5; H, 5·8; S, 13·2%). An 80% yield of the corresponding *benzylsulphonylacetic acid* was obtained by hydrolysis with cold 10% aqueous sodium hydroxide, the greater part of the acid being precipitated by acidification of the alkaline solution and the remainder isolated by extraction with chloroform. It was slightly soluble in benzene and soluble in acetone and water, whence it crystallised in plates, m. p. 139—140° (Found: C, 50·5; H, 4·7; S, 14·7. $C_9H_{10}O_4S$ requires C, 50·5; H, 4·7; S, 15·0%). A nearly theoretical yield of methylbenzylsulphone was isolated when the acid was heated at 180—190° until no further carbon dioxide was evolved.

(C) *Properties of α-Benzylsulphonyl-γ-ethylsulphonyl-Δ^α- and -Δ^β-propene.*—(i) The sulphones were soluble in chloroform, less so in ethyl acetate, alcohol, and water, and practically insoluble in ether. Although alkaline permanganate solution was reduced, no addition of halogen acid, halogens, or sulphuric acid took place. They could be distilled without decomposition (b. p. above 220°/0·1 mm.), but no separation of isomerides resulted.

(ii) *Separation of the Δ^α- and the Δ^β-isomeride.* The procedure followed for the separation was to recrystallise the crude product from ethyl acetate. Part of the solvent of the filtrate was removed by evaporation in a vacuum, and excess of petrol (b. p. 40—60°) added to the residue. The precipitate, consisting mainly of the Δ^α-sulphone, was rapidly recrystallised three times from benzene, from which it separated in plates, m. p. 105—107° (Found: C, 50·3; H, 5·6; S, 21·9%). Further recrystallisation usually caused isomerisation with a consequent lowering of the melting point.

The crude Δ^β-sulphone from the first ethyl acetate crystallisation was recrystallised a further three times from ethyl acetate and then from benzene, from which it was obtained in needles, m. p. 131—132°, having a typical soapy feel when crushed with a spatula. This was the highest m. p. usually recorded, but in one case, only, after crystallisation from a very dilute benzene solution the substance had m. p. 137° (Found: C, 49·8; H, 5·4%). The yield from 15 g. of a mixture, m. p. 95—100°, was 0·5 g. of the Δ^α-sulphone and 2·0 g. of the Δ^β-sulphone, the remaining 12·5 g. being a mixture (Found: C, 50·1; H, 5·6%) of the two which could again be partly separated by the same cycle of operations.

(iii) *Catalytic reduction.* The sulphones (1 g.), dissolved in glacial acetic acid, were shaken with Adams's catalyst in the presence of hydrogen until no more absorption took place. The resulting α-benzylsulphonyl-γ-ethylsulphonylpropane was identical (m. p. and mixed m. p.) with that described in section B (i) (Found: C, 50·0; H, 6·4; S, 21·8%).

(iv) *Condensation with benzaldehyde.* Either of the sulphones (2 g.) was shaken with benzaldehyde (6 c.c.) and piperidine (3 drops). The solution became warm and water was eliminated. The cloudy solution was kept for 12 hours, and the *βδ-benzylsulphonylethylsulphonyl-α-phenylbutadiene* (IV) precipitated by the addition of excess of ether. It crystallised from ethyl acetate in fine needles, m. p. 154° (Found: C, 60·4; H, 5·3; S, 17·2; *M*, 379. $C_{19}H_{20}O_4S_2$ requires C, 60·6; H, 5·3; S, 17·0%; *M*, 376).

Complete reduction of the condensation product could not be effected. It was recovered unchanged when treated with hydrogen and Adams's catalyst at ordinary pressures, and boiling under reflux with hydriodic acid (*d* 1·94) for 6 hours appeared to give a *dihydro-compound*, which crystallised from ethyl acetate–petrol (b. p. 60—80°) in needles, m. p. 124° (Found: C, 60·6; H, 5·8; S, 16·4. $C_{19}H_{22}O_4S_2$ requires C, 60·3; H, 5·8; S, 16·9%).

(v) *Equilibration experiments.* A melting-point diagram was constructed from artificial mixtures of the two sulphones. Since an experimental mixture had of necessity to be melted before the composition could be determined, the artificial mixtures were similarly fused and allowed to solidify before determination of the melting point was carried out. This made an automatic allowance for the interconversion that takes place during fusion, and accounts for the rather low melting points of the pure sulphones recorded in the table below:

Melting Points of Mixtures of the Δ^α- with the Δ^β-Sulphone.

Δ^β-Sulphone, %	100	72·1	50·0	37·0	24·1	16·9	0·0
M. p.	126·3°	117·7°	108·5°	101·0°	91·5°	95·0°	103·5°

The following interconversion experiments were recorded :

(a) The Δ^{β}-sulphone (m. p. 131°, 0·1 g.) was boiled under reflux for 2 days with methyl alcohol (10 c.c.), and the solution evaporated to dryness. The residue had m. p. 105°, corresponding to 44% of the Δ^{β}-sulphone. This figure was confirmed by the addition of a known quantity of the isomeride to the mixture and redetermination of the m. p.

(b) The Δ^{β}-sulphone (1·0 g.) was boiled with methyl alcohol for 24 hours. The residue after removal of the solvent had m. p. 103·5°, corresponding to 41·2% of the Δ^{β}-sulphone.

(c) The Δ^{α}-sulphone (0·1 g.) was boiled with benzene (10 c.c.) for 2 days, it then having m. p. 105·5°, equivalent to 44·8% of the Δ^{β}-sulphone. This was confirmed as in the case of (a).

(d) Experiment (b) was repeated, leading to 97° for the m. p. of the residue, equivalent to 31·5% of the Δ^{β}-sulphone.

The residues from (b) and (d) were subsequently used in the ozone experiments (section D).

(D) *Fission of* (I) *and* (II) *by Ozone.*—The essential requirement was the isolation of the benzyl- and ethyl-sulphonylacetic acids formed by the fission of the Δ^{α}- and the Δ^{β}-sulphone respectively from a mixture which contained in addition to these substances the corresponding sulphonic acids, sulphuric acid, benzyl- and possibly ethyl-sulphonylacetaldehyde, unchanged sulphone, and small quantities of formaldehyde and formic acid. Moreover it was found that, though fission did not occur in chloroform solution, it was difficult to prevent complete oxidation to the sulphonic acids when acetic acid was used. The method finally adopted was to pass ozonised oxygen through a water–chloroform solution of the sulphones for 16—24 hours. The chloroform layer contained the unchanged sulphones and benzylsulphonylacetaldehyde, identified by m. p. and by the *p*-nitrophenylhydrazone (Part III, *loc. cit.*) respectively. Ethylsulphonylacetaldehyde was not positively identified, but its presence was inferred from the low analysis figures obtained for the above nitrophenylhydrazone unless it was carefully purified.

The aqueous layer was heated on a water-bath and neutralised with excess of barium carbonate. After filtration, the filtrate was slightly acidified with hydrochloric acid and evaporated to dryness. The barium salts thus obtained were mixed with absolute ethyl alcohol and a slight excess of concentrated sulphuric acid and esterified by the alcohol vapour method. The esters were extracted from the diluted solution with chloroform and dried, and the solvent removed: the residue was heated on the steam-bath for 12 hours with concentrated hydrochloric acid. The acid solution was diluted, boiled with norit, and filtered, and the filtrate evaporated to dryness. The mixed acids were heated in a glycerol bath at 180—250° until decomposition was complete; the resulting sulphones, dissolved in chloroform, were washed with sodium bicarbonate solution and dried. Distillation of the solvent yielded a rather dark residue, which was purified by boiling with norit in ethyl acetate solution. The composition of the mixed sulphones was determined by a fusion curve of artificial mixtures of methylethyl- and methylbenzyl-sulphones. In each case the figure obtained was checked by addition of a known proportion of one of the constituents to the experimental mixture. The applicability of the method was confirmed by preliminary trials with artificial mixtures of benzyl- and ethyl-sulphonylacetic acids with the corresponding sulphonic acids.

M. p.'s of Mixtures of Methylbenzyl- and Methylethyl-sulphones.

Methylbenzylsulphone, %	0·0	9·4	20·2	34·1	48·7	65·7	82·0	100·0
M. p.	34·6°	32·0°	48·4°	66·2°	82·3°	99·0°	112·5°	125·6°

TABLE I.

Fission by Ozone of Mixtures of the Δ^{α}- and the Δ^{β}-Sulphone.

M. p. of mixture.	β-Sulphone, %.	Wt. taken, g.	Wt. of mixed sulphone, g.	Methyl-benzyl-sulphone, %.	M. p. of mixture.	β-Sulphone, %.	Wt. taken, g.	Wt. of mixed sulphone, g.	Methyl-benzyl-sulphone, %.
131°	100	1	0·02	97·5	103·5° *	41·2	1	0·02	74·0
125—126	95	1	0·10	95·1	97 *	31·5	1	0·06	62·7
117	68	3	0·22	75·0	95—100†	ca. 33·0	2	0·05	57·0
105—108	ca. 47	1	0·04	54·0	100—104	,, 40·0	2	0·25	41·0
95—100	,, 33	2	0·10	43·3					

* Equilibrated sulphones; cf. section C (v,b and v,d respectively). † Equilibrated sulphones.

(E) *Fission by Ozone of the Sulphide-sulphones* (VII).—These were carried out in exactly the same way as with the bis-sulphones. The results are in Table II.

TABLE II.

Fission of $R{\cdot}SO_2{\cdot}CH{:}CH{\cdot}CH_2{\cdot}SR'$.

R.	R'.	Wt. taken, g.	Wt. of mixed sulphones, g.	Methylbenzyl-sulphone, %.
Benzyl	Ethyl (VII)	1·0	0·08	47·0
,,	,, ,,	1·8	0·23	87·5
,,	,, ,,	1·0	0·05	91·0
Ethyl *	Benzyl (X)	1·9	0·15	70·0

* Benzaldehyde was found in the neutral fraction.

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65. *Influence of Poles and Polar Linkings on Tautomerism in the Simple Three-carbon System. Part V. The Course of Prototropic Change in the Bissulphonylpropenes.*

By EUGENE ROTHSTEIN.

IN the preceding paper (Part IV), it is shown that α-benzylsulphonyl-γ-ethylsulphonyl-Δ^{α}- and -Δ^{β}-propene (I and II) are tautomeric either when boiled with a solvent or on melting.

When these compounds are treated with alkali alkoxide, stable alkali metal derivatives are formed having the composition $C_{24}H_{31}O_8S_4X$ or $C_{36}H_{46}O_{12}S_6X_2$ according to the solvent used (X = K or Na). The sulphones obtained therefrom after acidification were not crystalline; the amorphous solids which were formed when the syrups were rubbed with ether were hygroscopic and became syrupy again when treated with a solvent. Analysis of the crude substances was necessarily only approximate, but it indicated that the metal had been replaced by water leading to the formula $C_{24}H_{32}O_9S_4$. Treatment of the metal derivatives with methyl iodide yielded similar substances with higher carbon and hydrogen contents. The substances did not contain alkoxyl, nor did they form derivatives characteristic of a hydroxyl group, and they remained unchanged when boiled with concentrated hydriodic acid. When they were heated to 100°, some decomposition took place and thereafter the sulphones no longer solidified. Since the metallic derivatives contained no extra oxygen, it follows that they were true substitution products and not addition compounds, *i.e.*, self-addition was consequent on their formation. It was subsequently confirmed that hydrogen was evolved when the bis-sulphones were shaken with " molecular " potassium in xylene.

It was evident that by reducing the large number of possible isomerides having the dimeric composition, a crystalline material might be isolated from the mixture, and this was realised when *αγ-bis(ethylsulphonyl)propene*, $Et{\cdot}SO_2{\cdot}CH{:}CH{\cdot}CH_2{\cdot}SO_2Et$, was dissolved in alkali alkoxide, and the metallic derivative isolated and decomposed by acid. In these circumstances, the syrupy mixture afforded a good yield of a crystalline sulphone, m. p. 94—98°, which had the composition of the bis-sulphone but with a molecular weight double that required for the monomeric substance. The rather low and indefinite melting point was probably due to the presence of more than one isomeride, as was suggested by the appearance of the crystals, but separation was not achieved. The remaining syrup was not identified. The metal derivative furnished a ***dimethylated dimeride***, $C_{16}H_{32}O_8S_4$, m. p. 160—161°, when boiled with methyl iodide.

β-Hydroxy-αγ-bis(ethylsulphonyl)propane also gave the dimeric sulphone after prolonged boiling with alkali alkoxide. It is concluded, however, that dehydration preceded the formation of the metal derivative and dimerisation, because the saturated bis-sulphones did not appear to contain a reactive methylene group. Neither the bis-sulphonyl-β-hydroxypropanes, $R{\cdot}SO_2{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2{\cdot}SO_2R'$, nor α-benzylsulphonyl-γ-ethylsulphonylpropane, $CH_2Ph{\cdot}SO_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}SO_2Et$, condensed with benzaldehyde, nor did

the latter form a potassio-derivative. Moreover, whilst the bis-sulphonylpropenes formed the polymerised product in the presence of dilute potassium methoxide solution containing less than 3% of the potassium necessary to react with the sulphone present, the hydroxy-bis-sulphonylpropanes were completely unchanged by this treatment, even after prolonged boiling. Finally polymerisation occurred in the absence of water, when, for instance, a benzene solution of the bis-sulphone was warmed with "molecular" potassium, or when it reacted with diazomethane in ether–chloroform solution.

Since the removal of the proton by alkoxide must produce the kinetically free anions,

$$R{\cdot}SO_2{\cdot}CH{:}CH{\cdot}\overset{-}{C}H{\cdot}SO_2R' \text{ and } R{\cdot}SO_2{\cdot}\overset{-}{C}H{\cdot}CH{:}CH{\cdot}SO_2R'$$

resonance between which leads to the formation of the mesomeric ion and thence to self-addition, it is clear that interchange between (I) and (II) cannot take place with these ions as intermediates. The bis-sulphonylpropenes must therefore be classed with systems where the tautomeric change operates according to Lowry's termolecular mechanism (J., 1927, 2554; cf. Ingold, Salas, and Wilson, J., 1936, 1328). This is analogous to the preservation of asymmetry of an optically active methylazomethine during its interconversion to the racemic form of its isomeride, an observation which was advanced by Hsü, Ingold, and Wilson as the first unambiguous case of such a mechanism (J., 1935, 1779).

Consequently, though the canonical structure $R{\cdot}SO_2{\cdot}\overset{H\cdot}{C}H{:}CH{\cdot}\overset{-}{C}H{\cdot}SO_2R'$ postulated in Part IV can be regarded as playing only a small part in the resonance of the molecule, it enables the completed change to take place with the removal of the proton from one carbon atom and the simultaneous recombination at another part of the system, a second molecule furnishing the rôle of both base and acid respectively.

It appeared that the formation of a methylated monomeric derivative could only be expected to take place in the presence of a kation which could combine with the anion formed by the action of the alkoxide, before mesomerisation occurred. This was realised when 0·1*N*-potassium methoxide was slowly added to a cold mixture of the sulphonylpropene with methyl iodide. Under these conditions *αγ-benzylsulphonylethylsulphonyldimethylpropene* was isolated in about 30% yield, the remaining product being the polymerised sulphone.

Experimental.

(A) *αγ-Bis(ethylsulphonyl)propene.*—Oxidation of β-hydroxy-αγ-bis(ethylthio)propane (Tschugajev, and Kobljansky, *Z. anorg. Chem.*, 1913, **83**, 18) with perhydrol furnished *β-hydroxy-αγ-bis(ethylsulphonyl)propane* in 89% yield. It was isolated from the water–acetic acid solution by evaporation to dryness on the steam-bath and crystallised from benzene or ethyl alcohol in needles, m. p. 113—114° (Found: C, 34·5; H, 6·6; S, 26·4. $C_7H_{16}O_5S_2$ requires C, 34·4; H, 6·6; S, 26·2%).

β-Chloro-αγ-bis(ethylsulphonyl)propane, obtained in 71% yield when the above sulphone (30 g.) was treated with phosphorus pentachloride (28 g.) in chloroform solution (200 c.c.), separated from benzene in fine needles, m. p. 81° (Found: C, 32·4; H, 5·8; Cl, 12·7; S, 24·7. $C_7H_{15}O_4ClS_2$ requires C, 32·0; H, 5·7; Cl, 13·5; S, 24·4%).

αγ-Bis(ethylsulphonyl)propene resulted when the chloro-compound (23 g.) was boiled under reflux with pyridine (25 c.c.) for 3 hours. It crystallised from benzene, in which it was not very soluble, in needles, m. p. 117—118° (Found: C, 37·1; H, 6·2; S, 28·2; *M*, 229. $C_7H_{14}O_4S_2$ requires C, 37·2; H, 6·2; S, 28·3%; *M*, 226). The bis-sulphone condensed with benzaldehyde in the presence of piperidine, yielding *βδ-bis(ethylsulphonyl)-α-phenylbutadiene*,

$$Et{\cdot}SO_2{\cdot}CH{:}CH{\cdot}C(SO_2Et){:}CHPh,$$

which crystallised in feathery needles, m. p. 137—139°, from ethyl acetate (Found: C, 52·9; H, 5·8; S, 20·5. $C_{14}H_{18}O_4S_2$ requires C, 53·5; H, 5·7; S, 20·4%).

(B) *Sodio- and Potassio-derivatives of αγ-Benzylsulphonylethylsulphonylpropene.*—(i) The bis-sulphone (3 g.) was mixed with 0·05*N*-sodium ethoxide (25 c.c.). The orange solution quickly deposited the *sodio*-derivative as a buff precipitate, which changed to red when exposed to air (Found: C, 47·7; H, 5·0; S, 21·1; Na, 3·4. $C_{24}H_{31}O_8S_4Na$ requires C, 48·2; H, 5·2; S, 21·4; Na, 3·8%). Repetition of the experiment with excess of *N*-sodium ethoxide yielded a *compound* containing 4·9% of sodium ($C_{36}H_{46}O_{12}S_6Na_2$ requires Na, 5·1%). The sodio-derivatives were partly hydrolysed by cold water, giving alkaline solutions.

(ii) The bis-sulphone (1·75 g.) was boiled under reflux with *N*-potassium *iso*propoxide (7 c.c.) for 1½ hours, and the precipitate collected and washed with *iso*propyl alcohol (Found : C, 45·9; H, 5·4; S, 20·4; K, 8·4. $C_{36}H_{46}O_{12}S_6K_2$ requires C, 46·0; H, 4·9; S, 20·4; K, 8·3%). When ethyl alcohol was used as the solvent, a *potassium* derivative of the dimeric sulphone resulted (Found : C, 46·8; H, 5·2; S, 20·8; K, 6·4. $C_{24}H_{31}O_8S_4K$ requires C, 46·9; H, 5·0; S, 20·8; K, 6·4%)

(iii) In order to confirm the reality of the two series of metallic derivatives, parallel experiments with *N*-solutions of the alkoxides were carried out; in each case the sulphone (0·3 g.) was boiled under reflux for 7 hours with *N*-alkoxide solution (5 c.c.), and the resulting derivative washed with the appropriate alcohol and analysed :

Alkoxide.	Colour of derivative.	Metal, %.	Calc. for $C_{21}H_{31}O_8S_4X$.	Calc. for $C_{36}H_{46}O_{12}S_6X_2$.
KOPr	Buff	7·5	K = 6·4%	K = 8·3%
KOMe	White	6·4		
NaOPr	Buff	4·9	Na = 5·1%	Na = 3·9%
NaOMe	White	4·2		

(C) *Sulphones from Metallic Derivatives.*—(i) The dimeric sodio-derivative was decomposed by carbon dioxide in alcohol–chloroform suspension. No acid was formed, but when excess of petrol was added to the filtered solution a *dimeric sulphone* was obtained, which separated from benzene–petrol (b. p. 40—60°) as an amorphous solid, m. p. *ca.* 83° (decomp.) (Found : C, 48·7; H, 5·8; S, 21·0; *M**, 643. $C_{24}H_{32}O_9S_4$ requires C, 48·6; H, 5·7; S, 21·6%; *M*, 592).

(ii) The sodio-derivative was boiled under reflux with methyl iodide in ethyl alcohol until solution was complete. The usual amorphous solid was obtained when the sulphone was mixed with ether. As with all these polymeric sulphones, the addition of most solvents caused the substance to become syrupy; an exception was *iso*propyl alcohol, but even in this case it separated from its solution in this solvent as an oil which solidified on scratching. Analysis showed that the sulphone was probably a *tetramethylated dimeride* (Found : C, 53·1; H, 6·1; S, 19·9; OEt, 0. $C_{28}H_{40}O_8S_4$ requires C, 53·2; H, 6·3; S, 20·3%).

(iii) The bis-sulphone (2 g.) was boiled under reflux with *N*-lithium ethoxide (7 c.c.). A red solution was formed, but only a slight precipitate. Excess of methyl iodide was added, and the heating continued for a further 1½ hours. The product appeared to be a *trimethylated trimeric sulphone*; it separated from *iso*propyl alcohol as an amorphous solid, indef. m. p. 65° and decomposing at 100°. Analysis indicated the presence of an extra molecule of water (Found : C, 50·8; H, 6·2; S, 20·1; *M*, 859. $C_{39}H_{56}O_{13}S_6$ requires C, 50·8; H, 6·1; S, 20·8; *M*, 924).

(iv) The sulphones obtained from the potassio-derivatives were similar to those described above. They all had indefinite m. p.'s and lost solvent at about 85°. Similar analysis figures were obtained whether the sulphone was heated above its m. p. in a vacuum until decomposition was complete (Found : C, 48·7; H, 5·7; S, 21·6%; *M*, 517), or allowed to separate from its solution in a large quantity of ether (Found : C, 48·9; H, 5·7; S, 21·9%; *M*, 532).

(v) Potassium (0·1 g.) was "molecularised" under benzene (5 c.c.), and the bis-sulphone (0·5 g.), dissolved in hot benzene (5 c.c.), added; hydrogen was evolved. The liquid, after boiling for 1 hour under reflux, was acidified by the gradual addition of glacial acetic acid (0·5 c.c.). The resulting sulphone was exactly similar to those described above (Found : *M*, 587).

(D) *Action of Alkoxides on αγ-Bis(ethylsulphonyl)propene.*—(i) The *sodio-* and *potassio-*derivatives were prepared as before (Found : C, 35·9; H, 5·7; S, 26·2; Na, 5·2. $C_{14}H_{27}O_8S_4Na$ requires C, 35·5; H, 5·7; S, 27·0; Na, 4·9%. Found : C, 34·6; H, 5·5; S, 26·1; K, 7·5. $C_{14}H_{27}O_8S_4K$ requires C, 34·3; H, 5·5; S, 26·1; K, 7·9%).

(ii) The sodio-derivative was decomposed by formic acid, and the sulphone rubbed with ether–ethyl acetate, yielding the *dimeride* of αγ-bis(ethylsulphonyl)propene, which after crystallisation from benzene separated from ethyl acetate–petrol (b. p. 60—80°) in mixed prisms, m. p. 94—95°; yield, *ca.* 55% (Found : C, 37·4; H, 6·3; S, 28·2; *M*, 435, 445. $C_{14}H_{28}O_8S_4$ requires C, 37·2; H, 6·2; S, 28·3%; *M*, 452).

(iii) The *dimeride* of *αγ-bis(ethylsulphonyl)-α(?)-methylpropene* was formed when *N*-sodium ethoxide (7 c.c.) was gradually added to a boiling solution of the bis(ethylsulphonyl)propene (0·5 g.) in methyl iodide. The resulting syrupy *sulphone*, when treated with methyl alcohol–ether, afforded a small quantity of crystalline material, which separated from ethyl acetate in

* The molecular weights, determined by Rast's method, are of necessity minimum figures for these substances owing to the difficulty of purification. There is therefore the probability that some of them are mixtures of dimeric and trimeric sulphones.

prisms, m. p. 160—161° (Found: C, 39·9; H, 6·6; S, 27·0; *M*, 511. $C_{16}H_{32}O_8S_4$ requires C, 40·0; H, 6·7; S, 26·7%; *M*, 480).

(E) *Action of Alkoxide on the Hydroxy-bis-sulphonylpropanes.*—(i) β-Hydroxy-α-benzylsulphonyl-γ-ethylsulphonylpropane (2 g.) was boiled under reflux with *N*-potassium ethoxide (12 c.c.), the yellow solution gradually depositing the potassio-derivative (Found: C, 46·3; H, 5·4; S, 21·8; K, 6·3%). It was not produced when small concentrations of alkoxide were used, the original sulphone being recovered unchanged. The corresponding propene, on the other hand, gave the polymerised sulphone when boiled with 0·1*N*-sodium methoxide for 30 minutes (Found: *M*, 532. See section C, iv).

(ii) β-Hydroxy-αγ-bis(ethylsulphonyl)propane (0·7 g.) gave a dark brown solution when boiled with *N*-potassium methoxide (5 c.c.), no solid being precipitated. The semi-solid, dark brown product obtained from the solution was purified by boiling with norit in ethyl acetate and isolated in 50% yield by careful precipitation with ether. Two recrystallisations from ethyl acetate–petrol afforded mixed prisms, m. p. 95—98°. It was not identical with the dimeride previously obtained (section D, ii), since the m. p. was lowered to 90° when the two were mixed (Found: C, 37·1; H, 6·3; S, 28·3%; *M*, 490).

(F) *Methylation of Benzylsulphonylethylsulphonylpropene.*—(i) 0·1*N*-Sodium methoxide (40 c.c.) was slowly added to a cold stirred suspension of the bis-sulphone (2·0 g.) and methyl iodide (20 c.c.) in methyl alcohol (20 c.c.), the sulphone gradually dissolving. The mixture was boiled under reflux for 5 minutes, diluted with water, and extracted with chloroform. Removal of the solvent yielded a semi-solid which, after washing with methyl alcohol, afforded *α-benzylsulphonyl-γ-ethylsulphonyldimethylpropene* in about 50% yield; this crystallised from ethyl acetate–petrol (b. p. 60—80°) in needles, m. p. 135—136° (Found: C, 53·2; H, 6·4; S, 20·2; *M*, 262, 267, 338. $C_{14}H_{20}O_4S_2$ requires C, 53·2; H, 6·3; S, 20·3%; *M*, 316).

The corresponding hydroxybis-sulphonylpropane was unchanged by this treatment.

(ii) The bis-sulphone (1 g.) was dissolved in chloroform, and ethereal diazomethane (from 2 c.c. of nitrosomethylurethane) added. Nitrogen was evolved and the mixture grew warm. The residue left when the solvent was distilled contained nitrogen, and had all the properties of the polymerised sulphones. The bis-sulphone had undoubtedly been methylated, since the analysis figures for the substance after it had been heated in a vacuum showed that the carbon content was much greater than would be required for the simple addition of diazomethane to give the pyrazolone derivative (Found: C, 52·3; H, 5·3; S, 16·9; N, 8·2%).

The analyses in this and the preceding paper were carried out by Dr. Ing. A. Schoeller of Berlin or Dr. G. Weiler of Oxford.

The University, Leeds. [*Received, December 8th, 1936.*]

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66. *The Azo-group as a Chelating Group. Part II. The Structure of the Diazoamino-compounds.*

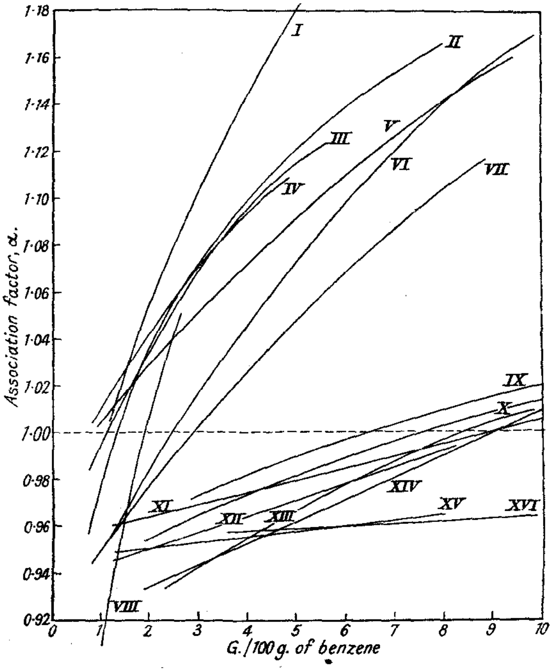
By Louis Hunter.

The constitution of the diazoamino-compounds, since their discovery by Griess (*Annalen*, 1862, **121**, 258), has presented an unsolved problem. The fundamental difficulty is the fact, originally revealed by Griess (*Ber.*, 1874, **7**, 1618), that the unsymmetrical compounds are capable of synthesis by interaction between a diazonium salt and a primary amine by the two alternative routes:

$$R{\cdot}N_2X + R'{\cdot}NH_2 \longrightarrow R{\cdot}N_3H{\cdot}R' \longleftarrow R{\cdot}NH_2 + R'{\cdot}N_2X$$

Similarly, fission of the compound so prepared (*e.g.*, by acids) usually results in the formation of all four possible products. Attempts to decide for each individual diazoamino-compound whether it possesses the formula R·N:N·NHR′ or R·NH·N:NR′ have, in most cases, led to conflicting results (for summary of evidence, see Saunders, "The Aromatic Diazo-Compounds and Their Technical Applications," pp. 131 *et seq.*, 1936). It is now fairly generally agreed that the unsymmetrical diazoamino-compounds are chemically homogeneous, and that the case is one of "virtual tautomerism" (von Pechmann, *Ber.*, 1895, **28**, 869; Ingold and Piggott, J., 1922, **121**, 2381).

Whatever be the structure of the diazoamino-compounds, however, that of their *N*-substituted derivatives is beyond dispute, for two different isomers R'·N:N·NRR" and R·N:N·NR'R" can in all cases be readily synthesised. In the present investigation measurements have been made of the molecular weights of diazoamino-compounds in benzene solution, and the results clearly show that, although substances of formula R·N_3H·R' are associated in solution, those of formula R'·N_3·RR" are of normal molecular weight. The data are in the tables, and when plotted graphically (see figure), the results



indicate a wide divergence of type between *N*-substituted and unsubstituted diazoamino-compounds. The curves due to the former (curves IX—XVI) lie for the most part slightly below the line indicating normal molecular weight; those of the latter (curves I—VIII) lie above, and are invariably steeply sloped, indicating a rapidly rising degree of association with increasing concentration. *pp'*-Diethoxydiazoaminobenzene (curve VIII) is very abnormal in showing an apparent dissociation in dilute solution, but the slope of the curve is such as clearly to indicate that, were it possible to obtain a more concentrated solution, it would undoubtedly show considerable association. That the abnormality is not due to the presence of alkoxy-groups is shown by the fact that it is not shared by *N*-substituted diazoamino-compounds containing methoxy-groups (curves X and XV).

Unsubstituted diazoamino-compounds.

Figures in parenthesis indicate the normal molecular weight; *M* is the apparent molecular weight. Concentrations are given as g./100 g. of benzene; α is the association factor.

Compound	Concn.	*M.*	α.
Diazoaminobenzene (197) (Curve VI)	1·07	188·0	0·954
	2·54	198·8	1·010
	4·68	209·6	1·064
	8·10	222·5	1·130
	9·88	230·1	1·168
p-Methyldiazoaminobenzene (211) (Curve V)	0·93	211·9	1·004
	2·91	220·7	1·046
	4·68	229·4	1·086
	7·44	238·2	1·130
	9·31	244·9	1·160
op′-Dimethyldiazoaminobenzene (225) (Curve III)	0·77	222·0	0·986
	2·26	235·1	1·045
	3·93	245·9	1·093
	5·55	252·1	1·120
mp′-Dimethyldiazoaminobenzene (225) (Curve II)	0·70	215·9	0·959
	1·77	231·5	1·030
	3·28	243·1	1·080
	5·46	254·2	1·130
	7·97	261·8	1·163
pp′-Dimethyldiazoaminobenzene (225) (Curve IV)	0·78	225·6	1·003
	2·79	239·6	1·065
	4·75*	247·6	1·100
pp′-Dimethoxydiazoaminobenzene (257) (Curve I)	1·17	258·2	1·005
	2·64	283·0	1·101
	4·03	294·5	1·146
	5·90	307·2	1·195
	7·14	318·4	1·239
oo′-*Dimethoxydiazoaminobenzene* (257) (Curve VII)	0·76	242·4	0·943
	2·26	252·8	0·984
	3·84	263·0	1·024
	5·56	270·8	1·054
	7·57	281·4	1·095
	8·72	286·9	1·116
pp′-Diethoxydiazoaminobenzene (285) (Curve VIII)	0·67	236·0	0·828
	1·21	261·8	0·919
	1·69	276·2	0·969
	2·56*	299·0	1·050

N-*Substituted diazoamino-compounds.*

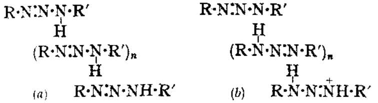
Compound	Concn.	*M.*	α.
1-*p*-Tolyl-3 : 3-dimethyltriazen (163) (Curve XII)	1·27	154·3	0·947
	3·59	156·7	0·961
	5·23	159·1	0·976
	8·14	162·0	0·994
1-m-*Tolyl-3-phenyl-3-methyltriazen* (225) (Curve XI)	1·27	216·3	0·961
	3·39	218·5	0·971
	6·00	220·5	0·980
	8·21	224·2	0·997
	10·73	226·5	1·007
1-p-*Bromophenyl-3 : 3-dimethyltriazen* (228) (Curve XIII)	2·33	213·0	0·934
	5·48	222·0	0·974
	7·86	227·2	0·996
	9·90	229·8	1·008
1-p-*Bromophenyl-3-phenyl-3-methyltriazen* (290) (Curve IX)	2·98	279·6	0·964
	4·09	286·5	0·988
	6·10	290·0	1·000
	8·37	293·7	1·013
	10·62	296·1	1·021
1-p-*Bromophenyl-3-phenyl-3-benzyltriazen* (366) (Curve XVI)	3·51	351·5	0·960
	5·41	349·6	0·955
	7·66	350·7	0·958
	9·89	354·1	0·968
p-Bromophenylazopiperidine (268) (Curve XIV)	1·96	250·4	0·934
	4·94	257·9	0·962
	7·78	264·2	0·986
	10·34	270·7	1·010
1-o-*Methoxyphenyl-3-phenyl-3-methyltriazen* (241) (Curve XV)	1·32	228·6	0·948
	2·81	229·0	0·950
	4·40	231·8	0·962
	7·77	232·0	0·963
1-p-*Methoxyphenyl-3-phenyl-3-methyltriazen* (241) (Curve X)	1·88	229·9	0·954
	4·51	237·2	0·984
	7·37	240·3	0·997
	10·66	244·7	1·015

* The substance was not sufficiently soluble for measurements to be made at higher concentrations.

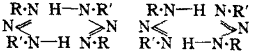
It is clear from these results that the association of substances of formula $R{\cdot}N_3H{\cdot}R'$ is due to the presence of the imino-hydrogen atom, and it seems reasonable to attribute it to hydrogen-bond formation; *i.e.*, adjacent molecules are held together by sharing the imino-hydrogen atom, the alternative point of attachment probably being at one of the azo-nitrogen atoms. The molecular-weight measurements give no information as to the extent of the association, and there are two types of polymer possible, *viz.*, open-chain, of the kind suggested for water and other hydroxy-compounds (*Ann. Reports*, 1934, **31**, 42) and for quinhydrone (Foz and Palacios, *Anal. Fís. Quím.*, 1932, **30**, 421), or cyclic, for which, on steric grounds, the most probable form is dimeric. It is possible that in solution both types of polymer are present.

By using the newer concept of hydrogen bonds (Sidgwick, *Ann. Reports*, 1933, **30**, 112) it at once becomes apparent that the association of the diazoamino-compounds probably has an intimate bearing on their tautomeric behaviour. The following formulæ depict the extreme forms (*a*) and (*b*) due to hydrogen resonance in an open-chain polymer (I) and in a cyclic polymer (II). Such a formulation implies that the imino-hydrogen atoms are attached alternately to nitrogen atoms in adjacent molecules, with a consequent rearrangement of valency linkings within the remainder of the molecule. It is probable that in the undissolved condition the diazoamino-structure is represented by either (I) or (II) or some

variant of these. In solution, however, partial dissociation occurs, each extreme resonance state giving rise to a different unimolecular form; *i.e.*, (I*a*) and (II*a*) dissociate into



(*a*) (*b*) (I.)



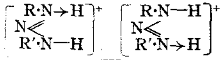
(*a*) (*b*) (II.)

R·N:N·NH·R′, and (I*b*) and (II*b*) into R·NH·N:N·R′. Such a view would lead us not only to accept, but indeed to expect, the mass of conflicting evidence for any static formulation of the diazoamino-compounds. There is obviously the possibility of numerous other less symmetrical variations of the two general types of polymer represented above. Whatever the actual dispositions of the constituent molecules within the polymers, however, they will one and all dissociate into mono-molecules which will show the properties of both R·N:N·NH·R′ and R·NH·N:N·R′.

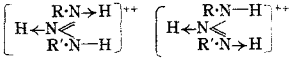
The dimeric form (II) is chosen as the most probable type of cyclic polymer on stereochemical grounds. The *trans*-configuration of diazoamino-compounds has long been accepted in explanation of their stability; and this, together with the 180° valency angle of the co-ordinated hydrogen atom (Sidgwick, *loc. cit.*, pp. 113—115), results in a practically strainless eight-membered ring (compare the dimeric form of carboxylic acids; Pfeiffer, "Organische Molekülarverbindungen," 2nd edn., 1927, pp. 122, 123; Sidgwick, *loc. cit.*).

With certain reagents the diazoamino-compounds react as though they possess a fixed and not a tautomeric constitution, and such reagents have been used diagnostically. For instance, their behaviour with phenyl *iso*cyanate led Goldschmidt and his co-workers (*Ber.*, 1888, **21**, 1016, 2557; 1905, **38**, 1096) to the conclusion that the imino-group is always attached to the more negative radical. On the other hand, the decomposition of diazoamino-compounds with ice-cold mineral acid led Dimroth and his co-workers (*Ber.*, 1905, **38**, 670; 1907, **40**, 2390) to the opposite conclusion. Such reactions find ready explanation as a preferential reaction of the diagnostic reagent with one of the unimolecular forms, the continuous removal of which ultimately results in the complete conversion of the less into the more reactive form.

The mild salt-forming properties of the diazoamino-compounds are probably attributable to a cause similar to that operating in their association, *viz.*, the tendency of the azo-nitrogen atoms to share electrons with, in this case, a hydrogen ion. These salts are very unstable, and may contain one or two (but never more) equivalents of acid to each molecule of diazoamino-compound, thus pointing to electron-donor properties only in the azo-nitrogen atoms. Formula (III) depicts the extreme states, due to hydrogen resonance, of the ion derived from a diazoamino-compound acting as a monoacid base, *e.g.*,



(III.)



(IV.)

$(Ph{\cdot}N_2{\cdot}NHPh)_2,H_2PtCl_6$ (Griess, *Annalen*, 1862, **121**, 261), and formula (IV) the ion derived from a diazoamino-compound acting as a diacid base, *e.g.*, $(C_6H_4Me)_2N_3H,H_2PtCl_6$ (Griess, *loc. cit.*, p. 277). It is doubtless the intermediate formation of ions of this structure which precedes the decomposition of the diazoamino-compound $R{\cdot}N_3HR'$ by mineral acid into a mixture of diazonium salts ($R{\cdot}N_2X$ and $R'{\cdot}N_2X$) and amines ($R{\cdot}NH_2$ and $R'{\cdot}NH_2$).

Experimental.

Molecular weights were measured cryoscopically in benzene, the same Beckmann thermometer, and benzene from the same source being used for all the measurements. In view of the tendency to undergo decomposition in hot solvents which characterises certain diazoamino-compounds

(Earl, *Chem. and Ind.*, 1936, 192), special care was taken in their purification. Since the majority of the known *N*-substituted diazoamino-compounds are liquids, a number of new solid compounds have been synthesised for the purpose of this investigation.

Diazoaminobenzene, crystallised rapidly from alcohol, formed pale yellow plates, m. p. 99°. *p*-Methyldiazoaminobenzene, crystallised similarly, formed yellow needles, m. p. 90°.

op'-Dimethyldiazoaminobenzene requires special care in purification, since considerable amounts of the isomeric *p*-tolueneazo-*o*-toluidine are formed during its preparation. It was obtained first from benzene and ligroin as an undoubted mixture melting sharply at 109°. Repeated crystallisation from the same solvents ultimately raised the m. p. to 117—118°. It formed long, straw-yellow, silky needles.

mp'-Dimethyldiazoaminobenzene crystallised from benzene and ligroin in bright yellow, silky needles, m. p. 96°. *pp'*-Dimethyldiazoaminobenzene, crystallised rapidly from alcohol, formed yellow needles, m. p. 116°.

oo'-Dimethoxydiazoaminobenzene was prepared in the usual way by diazotising *o*-anisidine in dilute hydrochloric acid, and adding an equivalent quantity of *o*-anisidine dissolved in hydrochloric acid, followed by an excess of aqueous sodium acetate under mechanical stirring. The oil first formed rapidly solidified, and was filtered off, washed, and crystallised whilst still moist from alcohol. Rapid cooling of the alcoholic solution was necessary to minimise decomposition. The product formed pale yellow leaflets, m. p. 97° (Found: N, 16·2. $C_{12}H_{15}O_2N_3$ requires N, 16·3%).

pp'-Dimethoxydiazoaminobenzene, crystallised repeatedly from benzene and ligroin, formed liquorice-yellow prisms, m.p. 100°. *pp'*-Diethoxydiazoaminobenzene crystallised from benzene in orange prisms, m.p. 119—120°.

1-*p*-Tolyl-3 : 3-dimethyltriazen formed large, sweet-smelling, colourless plates from alcohol, m. p. 50—51°.

3-*Phenyl*-1-m-*tolyl*-3-*methyltriazen*.—A solution of *m*-toluidine (1 mol.) in hydrochloric acid was diazotised at 0°. During thorough mechanical stirring a solution of methylaniline (1 mol.) in hydrochloric acid was added, followed by an excess of aqueous sodium acetate; this precipitated an orange-coloured oil which soon solidified. The resulting yellow solid was filtered off, washed with water, and crystallised from alcohol. It formed bright yellow leaflets, m. p. 67° (Found: N, 19·0. $C_{14}H_{15}N_3$ requires N, 18·7%).

1-p-*Bromophenyl*-3 : 3-*dimethyltriazen*.—*p*-Bromoaniline was diazotised at 0° in hydrochloric acid solution with sodium nitrite, until the starch–iodide reaction was just positive. An excess of cooled, saturated, aqueous sodium acetate was then added to remove mineral acidity, followed by aqueous dimethylamine solution until the whitish precipitate no longer formed. The pale buff-coloured solid was then filtered off, washed, and crystallised whilst still moist from alcohol. It formed pale buff prisms, m. p. 62·5°, having the sickly sweet odour common to most aryldimethyltriazens (Found: N, 18·3; Br, 34·8. $C_8H_{10}N_3Br$ requires N, 18·4; Br, 35·1%).

1-p-*Bromophenyl*-3-*phenyl*-3-*methyltriazen*, prepared from diazotised *p*-bromoaniline and methylaniline, crystallised from alcohol in orange flakes, m. p. 82° (Found: N, 14·3; Br, 27·4. $C_{13}H_{12}N_3Br$ requires N, 14·5; Br, 27·6%).

1-p-*Bromophenyl*-3-*phenyl*-3-*benzyltriazen*, prepared from diazotised *p*-bromoaniline and *N*-benzylaniline, crystallised from alcohol in long, silky, orange needles, m. p. 111—112° (Found: N, 11·6; Br, 21·4. $C_{19}H_{16}N_3Br$ requires N, 11·5; Br, 21·8%).

p-Bromophenylazopiperidine formed pale orange leaflets from alcohol, m. p. 55° (Found: Br, 29·7. Calc.: Br, 29·8%).

1-o-*Methoxyphenyl*-3-*phenyl*-3-*methyltriazen*, prepared from diazotised *o*-anisidine and methylaniline, crystallised from alcohol in thick, deep yellow prisms, m. p. 97—98° (Found: N, 17·3. $C_{14}H_{15}ON_3$ requires N, 17·4%).

1-p-*Methoxyphenyl*-3-*phenyl*-3-*methyltriazen*, prepared from *p*-anisidine as above, crystallised from alcohol in brilliant yellow, silky needles, m. p. 61° (Found: N, 17·4. $C_{14}H_{15}ON_3$ requires N, 17·4%).

Grateful acknowledgment is made to Professor C. K. Ingold, F.R.S., and the referees for their helpful assistance.

University College, Leicester. [*Received, November 5th*, 1936.]

67. *Studies in Electrolytic Oxidation. Part IX. The Anodic Oxidation of Chromic Salts to Chromates.*

By R. F. J. Gross and A. Hickling.

The electrolytic oxidation of chromic salts to chromic acid and chromates was recorded by Regelsberger (*Z. angew. Chem.*, 1899, **12**, 1123; *Z. Elektrochem.*, 1899, **6**, 308; see also Elbs, *ibid.*, 1899, **6**, 388; Haüssermann, *Z. angew. Chem.*, 1893, **6**, 363), and later investigated by Müller and Soller (*Z. Elektrochem.*, 1905, **11**, 863; see also Levi and Ageno, *Atti R. Accad. Lincei*, 1906, **15**, ii, 549, 615); since that time investigation of the process has been mainly concerned with its industrial utilisation (Askenasy and Révai, *Z. Elektrochem.*, 1913, **19**, 344; McKee and Leo, *Ind. Eng. Chem.*, 1920, **12**, 16; Drozdov, *J. Gen. Chem. Russia*, 1933, **3**, 345; see also Roudnick, *Z. Elektrochem.*, 1929, **35**, 249; Takegami, *Bull. Chem. Soc. Japan*, 1930, **5**, 16) and little has been done to elucidate its mechanism. The process may be formulated as an electrical change involving the transfer of electrons, $Cr^{\cdot\cdot\cdot} + 4H_2O = CrO_4'' + 8H^{\cdot} + 3e$, or it may be supposed that oxygen is first formed at the anode and then brings about chemical oxidation. Neither of these simple views will account, however, for the recorded peculiar features of the oxidation, notably that the process only occurs efficiently in acid solution at a lead dioxide anode, and scarcely at all at an anode of smooth platinum. It appeared of interest, therefore, to reinvestigate the process and to see if any light could be thrown upon it by the theory of electrolytic oxidation developed in the previous parts of this series (Glasstone and Hickling, J., 1932, 2345, 2800; 1933, 829; 1934, 10, 1772, 1878; 1936, 820; Hickling, J., 1936, 1453).

Experimental.

The electrolytic apparatus consisted of two 150-c.c. beakers, forming the anode and cathode compartments respectively, connected together by a wide glass siphon containing electrolyte, the ends of the siphon being stopped by tight filter-paper plugs. This arrangement was found to have a reasonably low electrical resistance, but completely prevented mixing of anolyte and catholyte, and avoided the possibility of impurities introduced by the use of a porous pot. The anolyte was usually 100 c.c. of 0·1*M*-chromium potassium sulphate in 0·5*N*-sulphuric acid, and for the catholyte 100 c.c. of *N*-sulphuric acid were used in each case; the siphon was filled with either *N*-sulphuric acid or saturated potassium sulphate solution according to whether an acidic anolyte was used or not. For most of the experiments a rectangular platinum sheet anode of area 20 sq. cm. was used; this was mounted vertically, and rotated at 160 r.p.m. Prior to use, the anode was cleaned with warm concentrated hydrochloric acid, warm concentrated nitric acid, and water, and heated to redness. A platinum-foil cathode was employed. Current was supplied from a 40-volt battery through rheostats and a milliammeter. In each experiment 720 coulombs of electricity were passed, and the anode solution was then analysed. Except where otherwise stated, all electrolyses were carried out at room temperature, *i.e.*, *ca.* 20°.

A.R. Chromium potassium sulphate, $Cr_2(SO_4)_3,K_2SO_4,24H_2O$, and A.R. sulphuric acid were used for preparing the anolyte. Since the violet colour of the solution interfered to some extent with the observation of the end-point in the iodometric estimation of the chromate formed, the solutions were boiled and cooled before use, the colour being thereby changed to green. Check experiments showed that both the violet and the green solutions gave identical results on electrolysis. The quantity of electricity passed was such as to give 100 c.c. of 0·025*M*-chromate if the oxidation took place with 100% efficiency. After electrolysis, the chromate was estimated by strongly acidifying measured portions of the solution, adding excess potassium iodide, and titrating with standard thiosulphate. The efficiencies were in general reproducible to 1—2%.

Results.

(In the following experiments, a "stock solution" is one of 0·1*M*-chromium potassium sulphate in 0·5*N*-sulphuric acid.)

Influence of C.D.—The influence of *C.D.* was investigated by electrolysing a stock solution with the smooth platinum anode, various currents being employed. The following results were obtained:

C.D., amp./sq. cm.	0·02	0·01	0·005	0·0025	0·001	0·0005
Efficiency, %	1	1	2	4	29	35

It is seen that the efficiency of the oxidation at a smooth platinum anode in acid solution is very low at moderate *C.D.*'s, but becomes appreciable when the *C.D.* is greatly reduced.

Influence of Temperature.—The following results were obtained at a number of temperatures with the smooth platinum anode and stock solution at a *C.D.* of 0·01 amp./sq. cm.

Temperature	20°	31°	51°	58°	69°	88°
Efficiency, %	1	21	47	57	77	77

The efficiency evidently rises rapidly with increasing temperature.

Effect of Acidity and Alkalinity.—The effect of varying acidity and alkalinity is shown by the results below, the smooth platinum anode being employed with a *C.D.* of 0·01 amp./sq. cm. Solutions of 0·1*M*-chromium potassium sulphate were made up in 0·5*N*-sulphuric acid, water, and 0·5*N*-potassium hydroxide respectively. 1 G. of calcium carbonate was added to each 100 c.c. of the water solution to act as a buffering agent and prevent its becoming strongly acid on electrolysis. The alkaline solution was slightly turbid.

Medium.	0·5*N*-H_2SO_4.	H_2O.	0·5*N*-KOH.
Efficiency, %	1	63	77

It is apparent that the oxidation at a platinum anode is greatly favoured by working in neutral and alkaline solutions.

Influence of Anode Material.—In order to determine the influence of anode material, a stock solution was electrolysed with a *C.D.* of 0·01 amp./sq. cm. with various anodes, the size, shape, and apparent area of each being the same as that of the smooth platinum. Prior to use, the platinised platinum anode was cleaned and washed as above; it was then subjected to cathodic or anodic polarisation in *N*-sulphuric acid at a *C.D.* of 0·025 amp./sq. cm. for 1 hour, or its oxygen content controlled by rotating it in 0·01*N*-potassium permanganate in p_H 9 borate buffer for 30 minutes (see Glasstone and Hickling, J., 1932, 2347). These treatments yielded different results, which are recorded. The gas-carbon anode was washed with warm water before use. The lead dioxide anode was made from lead sheet and was anodically polarised at 0·025 amp./sq. cm. for 1 hour in *N*-sulphuric acid. The results are given below.

Anode material.	Efficiency, %.	Anode material.	Efficiency, %.
Smooth Pt	1	Platinised Pt:	
PbO_2	100	Cathodically polarised	97
Gas C	1	Controlled	53
		Anodically polarised	43

The lead dioxide anode gives the theoretical efficiency of oxidation, and the smooth platinum and the gas-carbon anode give very little chromate. The behaviour of platinised platinum is of particular interest, cathodic polarisation greatly increasing, and anodic polarisation decreasing, the oxidation efficiency. This is the opposite of what has been observed in some other cases of electrolytic oxidation (cf. Glasstone and Hickling, J., 1933, 830).

Influence of Concentration.—Experiments were made in which the concentration of chromium potassium sulphate in 0·5*N*-sulphuric acid was varied. The controlled platinised platinum anode was used with a *C.D.* of 0·01 amp./sq. cm. The results are below:

Concn. of $Cr_2(SO_4)_3,K_2SO_4$, *M*	0·02	0·05	0·1	0·2
Efficiency, %	20	36	53	66

The efficiency increases with increasing chromium-ion concentration.

Influence of Anions.—The effect of foreign anions was studied by carrying out electrolyses with stock solution to which various salts had been added. The controlled platinised platinum anode was used with a *C.D.* of 0·01 amp./sq. cm. The following results were obtained.

Substance added.	(None.)	KNO_3, 0·1*N*.	KH_2PO_4, 0·1*N*.	$KClO_4$, satd.	KF, 0·1*N*.	H_3BO_3, 0·1*N*.
Efficiency, %	53	61	62	64	76	50

It is seen that all the strong electrolytes increase the efficiency somewhat, the effect of fluoride being particularly marked, whereas boric acid has no appreciable effect.

To see if chromium salts other than the sulphate could be anodically oxidised to chromate, electrolyses were carried out with the nitrate in nitric acid, and the perchlorate in perchloric acid as electrolytes. The electrolytic conditions were as above, and the following results were obtained.

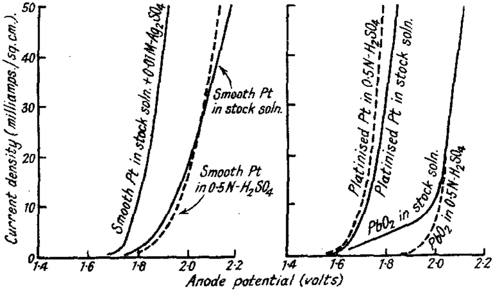
Electrolyte.	Efficiency, %.
0·1*M*-$Cr_2(SO_4)_3,K_2SO_4$ in 0·5*N*-H_2SO_4	53
0·2*M*-$Cr(NO_3)_3$ in 0·5*N*-HNO_3	60
0·2*M*-$Cr(ClO_4)_3$ in 0·5*N*-$HClO_4$	86

Influence of Catalysts for Hydrogen Peroxide Decomposition.—The influence of catalysts for hydrogen peroxide decomposition was found by adding various metallic sulphates and oxides to the anolyte. Two sets of experiments were carried out: (*a*) with the usual acid stock solution, and (*b*) with an initially neutral 0·1*M*-chromium potassium sulphate solution containing 1 g. per 100 c.c. of calcium carbonate to act as a buffering agent and prevent the solution becoming very acid on electrolysis. The smooth platinum anode was used with a *C.D.* of 0·01 amp./sq. cm.

Catalyst.	Efficiency, %. Acid solution.	Efficiency, %. Neutral solution.
(None)	1	63
$CuSO_4$, 0·01*M*	2	40
$FeSO_4$, 0·01*M*	2	27
$CoSO_4$, 0·01*M*	8	31
$MnSO_4$, 0·01*M*	7	17
,, 0·1*M*	19	
$PbSO_4$, satd.	70	96
Ag_2SO_4, 0·01*M*	97	87
,, 0·001*M*	95	
PbO_2, 0·5 g./100 c.c.	93	
MnO_2, 0·5 g./100 c.c.	5	

In general, oxide deposits were observed on the anode when electrolytes containing lead, manganese, or silver salts were used. It is to be noted that in acid solution all the catalysts for hydrogen peroxide decomposition raise the efficiency of the oxidation, the effect being particularly marked with lead and silver compounds; in neutral solution, however, except in the cases of lead and silver salts, the catalysts decrease the efficiency markedly. This peculiar result will be discussed later.

Potential Measurements.—In order to make measurements of the potentials at which the oxidation occurs, a small stationary platinum anode of area 0·1 sq. cm. was used, and its potential at a series of currents measured against that of a saturated calomel electrode by the potentiometer–voltmeter method. Experiments were carried out with (*a*) the smooth platinum anode in 0·5*N*-sulphuric acid, in stock solution, and in stock solution containing 0·01*M*-silver sulphate severally, (*b*) the anode coated with lead dioxide in 0·5*N*-sulphuric acid and in stock solution, and (*c*) the platinised anode in 0·5*N*-sulphuric acid and in stock solution. In each case the anode was pre-polarised at a *C.D.* of 0·02 amp./sq. cm. for 15 minutes in the solution to be used, in order that a steady state might be attained before observations were made. The potentials were then measured at a series of increasing *C.D.*'s, and immediately afterwards a repeat experiment was carried out. In general, the results were reproducible within about 2 centivolts. The values are given in the diagrams in the form of *C.D.*–potential curves, the potentials being expressed on the hydrogen scale.



Chemical Oxidation of Chromic Compounds.—The chemical oxidising action of the substances likely to be formed at an anode was investigated.

Oxygen. Gaseous oxygen was bubbled for 3 hours through boiling 0·1*M*-chromium potassium sulphate solutions made up in 0·5*N*-sulphuric acid, water, and 0·5*N*-potassium hydroxide severally. No trace of chromate was formed in any case.

Hydrogen peroxide. Quantities of 20-vol. hydrogen peroxide, containing available oxygen equivalent to that formed at an anode by the passage of 720 coulombs of electricity, were added

to 100-c.c. lots of 0·1*M*-chromium potassium sulphate made up in 0·5*N*-sulphuric acid, water (containing 1 g. of calcium carbonate), and 0·5*N*-potassium hydroxide severally, and the solutions boiled until all the peroxide was decomposed (as indicated by testing with titanium sulphate). The solutions were then examined for chromate, and the results expressed as efficiencies.

Medium.	Acid.	Neutral.	Alkaline.
Oxidation efficiency, %	0	12	29

Metallic peroxides. Quantities of silver (Ag_2O_2 prepared by Jirsa's method, *Z. anorg. Chem.*, 1925, **148**, 130), lead, and manganese peroxides, containing available oxygen equivalent to that formed in the electrolysis, were added to 100 c.c. portions of 0·1*M*-chromium potassium sulphate made up in 0·5*N*-sulphuric acid, water (containing 1 g. of calcium carbonate), and 0·5*N*-potassium hydroxide, and the mixtures boiled for 3 hours; the solutions were then filtered, and the chromate formed estimated.

	Oxidation efficiencies, %.		
	Acid.	Neutral.	Alkaline.
Ag_2O_2	87	23	10
PbO_2	42	15	47
MnO_2	14	4	8

Discussion.

The experimental results seem to indicate conclusively that the electrolytic oxidation of chromic ions to chromate is not a purely electrical, reversible process, represented by the equation $Cr^{\cdot\cdot\cdot} + 4H_2O = CrO_4'' + 8H^{\cdot} + 3e$. Such a process should be characterised by a definite oxidation–reduction potential, and provided that potential can be attained the oxidation should be largely independent of variable factors such as anode material, temperature, addition of catalysts, etc. In the present case the *C.D.*–potential curves show no sign of any definite potential associated with the reaction; on the contrary, the oxidation takes place efficiently at a platinised platinum anode at a low potential and scarcely at all at a smooth platinum anode at a much higher potential. Many other such anomalies can be quoted. The potentials at which the oxidation takes place seem to be merely oxygen evolution values. It may be noted that attempts to measure the static potential of the chromate–chromic ion system have given unsatisfactory results (see Winter and Moyer, *J. Amer. Chem. Soc.*, 1935, **57**, 1402; Kolthoff, *Chem. Weekblad*, 1919, **16**, 450; Luther, *Z. physikal. Chem.*, 1899, **30**, 653).

The simple view that oxygen is first formed at the anode and then brings about chemical oxidation seems equally unsatisfactory. The chemical experiments show that gaseous oxygen does not oxidise chromic ions, and the *C.D.*–potential curves show no substantial depolarisation for oxygen Even if it is supposed that the oxygen is activated in some way by the electrode material, it seems impossible to explain such results as the effect of acidity and alkalinity, the influence of pre-polarisation on the platinised platinum anode, and the fact that catalysts such as manganese, cobalt, and copper sulphates have opposite effects in neutral and in acid solution.

All the results, however, can be accounted for if the view is adopted that hydrogen peroxide is primarily formed at an anode in aqueous solution by the irreversible combination of discharged hydroxyl radicals, and if the observations are then interpreted in terms of the experimentally ascertained properties of this peroxide and the metallic peroxides which are known to be formed in certain circumstances. The chemical experiments show that hydrogen peroxide oxidises chromic ions to chromate in alkaline solution, also in neutral solution to a less extent, but in acid solution brings about no oxidation—on the contrary it reduces any chromate present. It would, therefore, be expected that ***under conditions such that no alternative oxidising agent is formed***, the efficiency of oxidation should be high in alkaline solution, less in neutral solution, and negligible in acid solution. This corresponds precisely to the observed efficiencies with a smooth platinum anode at moderate *C.D.*'s.

For a complete interpretation of the experimental results with various electrode materials and in the presence of catalysts for hydrogen peroxide decomposition, it is necessary to

take into account the observed oxidising action of the metallic peroxides which may be formed. The following schemes will represent the possibilities for alkaline or neutral, and for acid solutions.

Alkaline and neutral solutions.

$$2OH' + 2\oplus = 2OH \longrightarrow H_2O_2 \longrightarrow H_2O + O \longrightarrow \tfrac{1}{2}O_2 \text{ (Oxygen evolved)}$$

H_2O_2 ↓ Oxidises chromic ions to chromate.

O ↓ May oxidise chromic ions to chromate through formation of metallic peroxide.

Acid solution.

$$2OH' + 2\oplus = 2OH \longrightarrow H_2O_2 \longrightarrow H_2O + O \longrightarrow \tfrac{1}{2}O_2 \text{ (Oxygen evolved)}$$

H_2O_2 ↓ Reduces chromate to chromic ions.

O ↓ May oxidise chromic ions to chromate through formation of metallic peroxide.

From the first scheme it is seen that in neutral solution a catalyst for hydrogen peroxide decomposition should reduce the oxidation efficiency at a smooth platinum anode unless there is formed at the same time a metallic peroxide which is itself a better oxidising agent for chromic salts than is hydrogen peroxide. In agreement with this it is found that copper, cobalt, ferrous, and manganous sulphates all markedly reduce the oxidation efficiency in neutral solution; of these, only manganese gives a visible peroxide deposit on the anode, and, as shown experimentally, manganese peroxide in neutral solution has only comparatively slight oxidising action on chromic salts. On the other hand, silver and lead salts give rise to peroxide deposits on the anode, and these, although good catalysts for hydrogen peroxide decomposition, are themselves, as shown experimentally, excellent oxidising agents. The oxidation efficiency is therefore raised.

In acid solution, as depicted in the second scheme, the state of affairs is quite different. Here, not only does hydrogen peroxide not oxidise chromic salts, but it tends to reduce any chromate which may be formed. In acid solution, therefore, any factor tending to decompose hydrogen peroxide will tend to increase oxidation efficiency, and the maximum effect will be obtained if, at the same time, a metallic peroxide which is a good oxidising agent can be formed. From the experimental results this is seen to be the case. Silver, lead, and (to a less extent) manganese salts, all of which are catalysts for hydrogen peroxide decomposition and can form peroxides which are oxidising agents, increase the efficiency markedly; other catalysts, such as copper and cobalt salts, which do not form oxide deposits on the anode, increase it slightly.

The influence of anode material can be explained in a similar way. Lead dioxide, which is a good catalyst for hydrogen peroxide decomposition and also a good oxidising agent, gives the highest efficiency. Gas carbon is a fairly good catalyst for hydrogen peroxide decomposition but lacks oxidising properties and therefore gives a low efficiency. The case of platinum requires special mention. It seems probable that an oxide can be formed on the platinum surface which slowly oxidises chromic salts to chromate. With smooth platinum at ordinary temperatures the process is too slow to give an appreciable efficiency of oxidation at normal *C.D.*'s; at very low *C.D.*'s, however, a larger fraction of the anodic oxygen can be utilised in this way and the efficiency of oxidation increases. A similar result may be brought about by raising the temperature, whereby the process is accelerated and at the same time the decomposition of hydrogen peroxide is favoured.* Platinised platinum is a good catalyst for hydrogen peroxide decomposition, and presents an enormously increased area for the oxidation; hence, high efficiencies are observed. Cathodic polarisation increases the catalytic power of platinum for hydrogen peroxide decomposition, but anodic polarisation decreases it (Spitalsky and Kagan, *Ber.*, **1926**, **59**,

* It might be suggested that the increase in oxidation efficiency at low current densities or elevated temperatures is due to increased chance of diffusion of chromic salt to the anode. The *C.D.* employed, however, seems to be considerably less than that for limiting diffusion conditions, and the theory meets with many additional difficulties.

2905); it would, therefore, be expected that cathodic polarisation should favour, and anodic polarisation decrease, the oxidation efficiency in acid solution, as is found to be the case. It is interesting to note that poisoning of the platinised platinum electrode decreases the oxidation efficiency; with the stock solution and the controlled platinised platinum anode at a *C.D.* of 0·01 amp./sq. cm., the oxidation efficiency was reduced from 53 to 37% by making the platinising solution 0·01*M* with respect to mercuric chloride.

SUMMARY.

1. A comprehensive investigation has been made of the anodic oxidation of chromic salts: the influence of *C.D.*, of temperature, of acidity and alkalinity, of anode materials (smooth and platinised platinum, lead dioxide, and gas carbon), of concentration, of anions, and of catalysts for hydrogen peroxide decomposition, has been studied.

2. The current efficiency for the formation of chromate at a smooth platinum anode is high in alkaline and in neutral solutions, but negligible in acid solution, unless either very low *C.D.*'s are employed or the temperature is raised. Lead dioxide and platinised platinum anodes give good efficiencies in acid solution, the amount of oxidation in the latter case being greatly affected by previous treatment of the electrode; gas carbon gives a very low efficiency. Small amounts of the sulphates of copper, cobalt, iron, and manganese markedly lower the efficiency of oxidation at a smooth platinum anode in neutral solution, but in acid solution they increase it. Silver and lead sulphates raise the efficiency considerably in both neutral and acid solutions.

3. The anode potentials were measured under a variety of conditions, and appear to be merely oxygen evolution potentials. There seems to be no relation between anode potential and efficiency of oxidation.

4. It is shown that the observations made in the present work cannot be accounted for by a purely electrical oxidation mechanism, and an alternative theory, involving the primary formation of hydrogen peroxide at the anode, is advanced.

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68. *The Kinetic and Thermodynamic Activity of Protons and Deuterons in Water–Deuterium Oxide Solutions.*

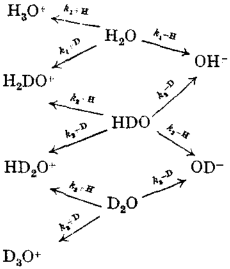
By W. J. C. ORR and J. A. V. BUTLER.

IT has been pointed out (Pedersen, *J. Physical Chem.*, 1934, **38**, 581) that if the primary step in catalysis by acids is supposed to be the formation of a complex of hydrogen ion and the substrate, two cases arise: (1) the rate of formation of the complex is great compared with the rate of the reaction, so that its concentration will be that determined by the thermodynamic equilibrium H^+ + substrate $\rightleftharpoons$ complex; (2) the rate of formation of the complex is small and becomes the rate-determining step of the reaction. In the former case the rate is determined by the concentration of the complex, which, depending on the thermodynamic equilibrium, will therefore be determined by the hydrogen-ion activity of the solution; in the latter, it will depend on the nature of the acids present in the solution. Hitherto the only means available of distinguishing the two cases has been to determine the catalytic activity of solutions containing acids other than H_3O^+, in order to ascertain whether there is any catalytic action apart from that due to the activity of hydrogen ions. This can only be achieved with rapid reactions which permit of measurements at very low hydrogen-ion activities. An alternative test has, however, been suggested by Gross and co-workers (*Trans. Faraday Soc.*, **1936**, **32**, 877). If the isotopic ratio of D : H is varied, in case (1) the change of the reaction rate will be proportional to the changes of the thermodynamic activity of the various hydrogen ions, but in case (2) this may fail.

Gross and his co-workers examined the dependence on the deuterium content of the solution of the rate of decomposition of diazoacetic ester and the hydrolysis of sucrose, obtaining the variation of the thermodynamic activity from the distribution of picric acid between water–deuterium oxide solutions and benzene. They found that the thermodynamic function agreed with the kinetic function in the diazoacetic ester reaction, but not with sucrose hydrolysis, and concluded that the former was of type (1), and the latter partly of type (2).

Hornel and Butler (J., 1936, 1361) recently determined the ratio of hydrolysis of acetal in hydrogen chloride solutions in water and in deuterium oxide, and showed that, by the use of buffers consisting of a weak acid and its salt, it was possible to determine the ratio of the dissociation constants of the acid in the two liquids. By the study of this reaction in solutions differing in deuterium content, it was thus possible (1) by using a strong acid at a constant concentration to determine the kinetic function of the rate on the isotopic composition of the water, (2) by similar measurements in formic acid–formate buffers to determine the variation of the dissociation constant of the acid, from which the thermodynamic function can be derived. Thus the same reaction serves to measure both the kinetic and the thermodynamic function.

Equilibrium in Water–Deuterium Oxide Mixtures, and the Activity of Protons and Deuterons.—In these solutions there are three neutral molecules, four positive ions, and two negative ions. All the possible equilibria between these species can be represented in terms of the following constants:



where $k_1^{+H} = [H_3O^+]/\alpha_{H^+}[H_2O]$, $k_1^{-H} = \alpha_{H^+}[OH^-]/[H_2O]$,
$k_3^{+D} = [D_3O^+]/\alpha_{D^+}[D_2O]$, $k_3^{-D} = \alpha_{D^+}[OD^-]/[D_2O]$, etc. . . . . (1)

The symbols in square brackets represent the activities of the various species. The proton and deuteron activities are indefinite and may be defined by putting

$$k_1^{+H} = 1,\ k_3^{+D} = 1;\ \textit{i.e.}\ \alpha_{H^+} = [H_3O^+]/[H_2O],\ \alpha_{D^+} = [D_3O^+]/[D_2O]$$

The various accessible equilibria between the species are obtained by combining two of these constants. There are a number of inter-relations between the constants. Thus, writing

$$[HOD]^2/[H_2O][D_2O] = K \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

and

$$\alpha_{H^+}^2[D_2O]/\alpha_{D^+}^2[H_2O] = L \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

we have

$$k_1^{+D}/k_2^{+H} = k_1^{-H}/k_2^{-D} = \sqrt{KL}$$
$$k_2^{+D}/k_3^{+H} = k_2^{-H}/k_3^{-D} = \sqrt{L/K} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

The total concentration of the isotopic hydrogen ions in the solution is

$$\Sigma H_3O^+ = H_3O^+ + H_2DO^+ + HD_2O^+ + D_3O^+$$
$$= (\alpha_{H^+}/f^+)\{[H_2O] + k_2^{+H}[HDO] + k_3^{+H}[D_2O] + (\alpha_{D^+}/\alpha_{H^+})[D_2O]\}$$

where f^+ is the activity coefficient of the hydrogen ions. Thus we obtain by (3)

$$\alpha_{H^+} = \Sigma H_3O^+ . f^+[H_2O]^{1/2}/Q'(n)$$

where

$$Q'(n) = [H_2O]^{3/2} + [HOD][H_2O]^{1/2}k_2{}^{+H} + [D_2O][H_2O]^{1/2}k_3{}^{+H} + [D_2O]^{3/2}/\sqrt{L} \quad . \quad (5)$$

Similarly, it can be shown that

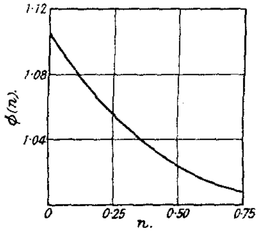
$$\alpha_{D^+} = \Sigma H_3O^+ . f^+[D_2O]^{1/2}/Q(n)$$

where $$Q(n) = Q'(n)\sqrt{L}$$

Now when $K = 4$, it has been shown that $[H_2O] = (1-n)^2$, $[D_2O] = n^2$, $[HOD] = 2n(1-n)$, where n is the fraction $D/(H + D)$. The best value of K at about 20° appears to be 3·27 (Topley and Eyring, *J. Chem. Physics*, 1934, 2, 220), and no simple expressions for $[H_2O]$, etc., can then be obtained, but the deviations from the values for $K = 4$ can be calculated and expressed by a function $\phi(n)$, such that

$$[H_2O] = (1-n)^2\phi^2(1-n) \, ; \, [D_2O] = n^2\phi^2(n) \quad . \quad . \quad . \quad . \quad . \quad (6)$$

Fig. 1.



Value of $\phi(n)$ *when* $K = 3{\cdot}27$.

The values of $\phi(n)$ for $K = 3{\cdot}27$ are shown in Fig. 1. Then

$$\alpha_{H^+} = \Sigma H_3O^+ . f^+ . (1-n)\phi(1-n)/Q'(n)$$
$$\alpha_{D^+} = \Sigma H_3O^+ . f^+ . n\phi(n)/Q(n) . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

Dissociation of Weak Acids in Isotopic Water Mixtures.—For the dissociation of a weak acid, HA, we need the additional constants

$$K_0 = [A^-]\alpha_{H^+}/[HA], \; K_1 = [A^-]\alpha_{D^+}/[AD]$$

Then $$[AH]/[AD] = K_1\alpha_{H^+}/K_0\alpha_{D^+} = K_1[H_2O]^{1/2}\sqrt{L}/K_0[D_2O]^{1/2}$$

and

$$\alpha_{H^+} = K_0\left(\frac{[AH] + [AD]}{[A^-]}\right)\left\{\frac{K_1\sqrt{L}[H_2O]^{1/2}}{K_1\sqrt{L}[H_2O]^{1/2} + K_0[D_2O]^{1/2}}\right\} \quad . \quad . \quad . \quad (8)$$

Introducing the value of α_{H^+} given in (5), and defining the dissociation constant in water containing a fraction n of deuterium as

$$K_n = \Sigma H_3O^+ . f^+[A^-]/\Sigma[HA]$$

we obtain

$$K_n = K_0Q'(n)\{K_1\sqrt{L}/(K_1\sqrt{L}[H_2O]^{1/2} + K_0[D_2O]^{1/2})\} \quad . \quad . \quad . \quad (9)$$

and

$$Q'(n) = K_n/K_0\{(1-n)\phi(1-n) + K_0Q'(1)/K_1 . n\phi(n)\} \quad . \quad . \quad . \quad (10)$$

Rates of Reactions Catalysed by Hydrogen Ions.—On the assumption that the rate is proportional to the proton and deuteron activities, we may write $\kappa_n = \theta_1\alpha_{H^+} + \theta_2\alpha_{D^+}$, where κ_n is the velocity constant in water of deuterium content n. By (7), we have

$$\kappa_n = \Sigma H_3O^+ . f^+/Q'(n) . \{\theta_1 . (1 - n)\phi(1 - n) + \theta_2 . n\phi(n)/\sqrt{L}\} \quad . \quad (11)$$

The rates in water and deuterium oxide respectively are

$$\kappa_0 = \theta_1\Sigma H_3O^+ . f^+ ; \ \kappa_1 = \theta_2\Sigma H_3O^+ . f^+ ;$$

so that, writing $\zeta_n = \kappa_n/\kappa_0$ for the ratio of the rate in a given solution to that in water at the same concentration of hydrogen ions, we have

$$\zeta_n = 1/Q'(n) \{(1 - n)\phi(1 - n) + \kappa_1/\kappa_0 . Q'(1)n\phi(n)\} \quad . \quad . \quad . \quad . \quad (12)$$

Similarly, in the presence of a weak acid and its salt,

$$\kappa_n = \theta_1\alpha_{H^+} + \theta_2\alpha_{D^+} = K_n/Q'(n)\{\theta_1 . (1 - n)\phi(1 - n) + \theta_2 . n\phi(n)/\sqrt{L}\} \Sigma AH/[A^-] . \quad (13)$$

Comparing solutions in which $\Sigma AH/[A^-]$ is kept constant, with solutions of the strong acid in which ΣH_3O^+ is kept constant, we obtain, on the assumption that the activity coefficients do not vary with the composition of the water,

$$\kappa_n/\kappa_0 = (K_n/K_0)\zeta_{n(HCl)} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (14)$$

from which the relative dissociation constants can be obtained.

Comparison of $Q'(n)$ from Kinetic and Thermodynamic Data.—In order to determine $Q'(n)$ from ζ_n, it is necessary to know $Q'(1) = 1/\sqrt{L}$. By (1) and (3), $L = [H_3O^+]^2[D_2O]^3/[D_3O^+]^2[H_2O]^3$, *i.e.*, the equilibrium constant of the reaction $2D_3O^+ + 3H_2O = 2H_3O^+ + 3D_2O$. Abel, Bratu, and Redlich (*Z. physikal. Chem.*, 1935, *A*, **173**, 360) have determined ΔE, the difference of the e.m.f. of the cells $H_2|HCl, H_2O, AgCl|Ag$ and $D_2|DCl, D_2O, AgCl|Ag$. This gives the free-energy change of the reaction

$$H_2 + 2H_2O + 2D_3O^+ + 2Cl^-_{(D_2O)} = D_2 + 2D_2O + 2H_3O^+ + 2Cl^-_{(H_2O)} (\Delta F = - RT \log K_A)$$

Combining this with the free-energy change of the reaction $H_2 + D_2O = D_2 + H_2O$ ($- RT \log K_B$), we obtain the free-energy change of

$$3H_2O + 2D_3O^+ + 2Cl^-_{(D_2O)} = 3D_2O + 2H_3O^+ + 2Cl^-_{(H_2O)} \ (\Delta F = - RT \log K_A/K_B)$$

This differs from $RT \log L$ by the difference of free energy of the chloride ions in deuterium oxide and in water. That such a difference exists is indicated by the different solubilities of salts in the two solvents, but sufficient data for evaluating this term have not been obtained. We have therefore identified L with K_A/K_B. Taking $K_A = 1{\cdot}3$ from Abel, Bratu, and Redlich, and $K_B = 1/3{\cdot}33^2$, we find that $L = 14{\cdot}4$, $Q'(1) = 0{\cdot}263$. Korman and La Mer's similar measurements (*J. Amer. Chem. Soc.*, 1936, **58**, 1396), with the quinhydrone in place of the hydrogen electrode, give, on the same assumption, $L = 15{\cdot}3$, $Q'(1) = 0{\cdot}256$. We shall adopt the value $Q'(1) = 0{\cdot}26$ for *ca.* 15°. Table I shows the velocity constants of the hydrolysis of acetal in 0·001348*N*-HCl–DCl solutions, with ζ_n and $Q'(n)$ calculated by (12), and Table II gives the velocity constants in half-neutralised solutions of formic acid, with the relative dissociation constants of formic acid given by (14) and $Q'(n)$ calculated by (10).

TABLE I.

Hydrolysis of acetal in 0·001348*N*-HCl–DCl *solutions.*

n	0·0	0·124	0·241	0·309	0·633	0·713	0·848	0·985	1·000
$10^3\kappa$	27·0	29·0	32·2	33·8	46·3	49·9	56·0		71·4 *
ζ_n	1·00	1·074	1·19	1·25	1·715	1·85	2·08	2·51	2·64
$Q'(n)$	1·00	0·90	0·79	0·73	0·48	0·43	0·36	0·28	0·26

TABLE II.

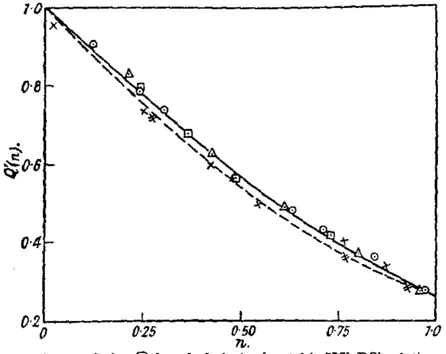
Relative dissociation constants of formic acid in H_2O–D_2O *solutions* (ionic strength = 0·01).

n	0·0	0·214	0·427	0·611	0·799	0·970	1·00
$10^3\kappa$	4·42	4·43	4·16	4·13	3·92	4·07	—
K_n/K_0	1·00	0·863	0·678	0·556	0·437	0·350	0·340 *
$Q'(n)$	1·00	0·83	0·62	0·49	0·36	0·27	0·26

* Extrapolated.

Fig. 2 shows that the $Q'(n)$ values obtained from the two sets of data are in excellent agreement with each other, proving that in this reaction the catalytic function is determined by the thermodynamic activity of the ions. Brönsted and Wynne-Jones's conclusion (*Trans. Faraday Soc.*, 1929, **25**, 39) that this reaction is a case of specific hydrogen-ion catalysis is thus confirmed by this method. The figure also shows the values of $Q'(n)$ derived from other data. La Mer and Chittum (*J. Amer. Chem. Soc.*, **1936**, **58**, 1642) have determined the dissociation constants of acetic acid at 25° in water–deuterium oxide mixtures by the direct conductivity method. The values calculated therefrom are somewhat lower than those given above. Gross's figures for the diazoacetic ester decomposition show excellent agreement with those of the acetal reaction, but his thermodynamic values, obtained from the distribution of picric acid, are on the whole distinctly lower.

FIG. 2.



$Q'(n)$ *obtained by various methods* : ⊙ *from hydrolysis of acetal in* HCl–DCl *solutions* ; △ *from relative dissociation constants of formic acid* ; ⊡ *from diazoacetic ester decomposition* (*Gross*) ; ≠ *from dissociation constants of acetic acid* (*La Mer and Chittum*) ; × *from picric acid distribution coefficients* (*Gross*).

The broken line in Fig. 2 shows the calculated value of $Q'(n)$ by (5) and (6) when $k_2{}^{+H} = 1$, $k_3{}^{+H} = 1$. This does not differ greatly from the experimental points, but better agreement is obtained with the values $k_2{}^{+H} = 1{\cdot}05$, $k_3{}^{+H} = 1{\cdot}10$, shown by the full line.

EXPERIMENTAL.

The reaction rates were determined by following the refractive index change in the reaction by a Hilger–Rayleigh interferometer, fitted with a water-jacketed chamber maintained at 15° ± 0·1°. The hydrogen chloride solutions were prepared from 0·001348*N*-deuterium chloride solution, made by adding *N*-hydrochloric acid to 99·9% deuterium oxide and an aqueous solution of hydrogen chloride of the same concentration. The intermediate solutions were prepared by mixing these solutions in various proportions by weight, and the deuterium content was calculated by assuming a linear variation in density between water and deuterium oxide and equality of their molar volumes. *N*/50-Formic acid solutions in both solvents were made from A.R. formic acid, and exactly half-neutralised by standard carbon dioxide-free sodium hydroxide and the intermediate solutions prepared by mixing in various proportions. The acetal had been freshly distilled from sodium carbonate and was free from acid. The deuterium oxide had been distilled and was neutral.

1 C.c. of the appropriate solution and 1 c.c. of the corresponding aqueous solution were placed in the compartments of the interferometer cell and left for 1 hour until temperature equilibrium was attained. The reading then taken checked the accuracy of the buffers and that of the deuterium content determination, since both with the formic acid and with the hydrogen chloride

solutions there was a linear relation between the interferometer reading and the deuterium content. 0·025 G. of acetal at 15° was now injected into the reading solution by means of a calibrated syringe, and thorough mixing obtained by shaking the whole water jacket and its contents. Satisfactory readings were obtained in 2—5 mins. after addition of acetal, and no spurious drift due to evaporation or other cause was observed in experiments lasting up to 24 hours. The velocity constants were obtained by plotting log $(r_\infty - r_t)$, where r = interferometer reading, against t, and excellent linearity was obtained, repeated experiments giving values of κ agreeing within 2%.

SUMMARY.

1. The rates of hydrolysis of acetal in $H_2O(HCl)$–$D_2O(DCl)$ mixtures have been determined, and this reaction has also been employed to determine the relative dissociation constants of formic acid in water–deuterium oxide solutions.

2. The possible equilibria between the three isotopic water molecules and the various isotopic ions have been formulated, and the function $Q'(n)$, which expresses the variation of the thermodynamic activity of protons (or deuterons) with the composition of the water, has been determined from the dissociation constants.

3. The rates of hydrolysis of acetal in solutions of hydrogen chloride and deuterium chloride give rise to the same function, and are therefore determined by the thermodynamic proton and deuteron activites of the solution.

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69. *The Kinetics of Bromine Addition to Olefinic Compounds.*

By P. W. ROBERTSON, N. T. CLARE, K. J. MCNAUGHT, and G. W. PAUL.

RECENT investigations have established in general terms the mechanism of bromine addition to ethylenic compounds. With effective impact the positive atom of the polarised bromine molecule attaches itself to the negative carbon of the ethylenic system; thereupon the resulting positive charge of the second ethylenic carbon atom is neutralised by the negative bromine ion, which has a momentary existence. Ionising solvents greatly accelerate the change, and, even if themselves only slightly ionised, provide a high local concentration of negative ions which will compete with the bromine ion for the positively charged carbon atom. For instance, in water the bromohydroxy-derivative may be formed almost exclusively (Read and Read, J., 1928, 745), and if an ion such as the nitrate ion is present in the solution, this is added in preference to hydroxyl (Francis, *J. Amer. Chem. Soc.*, 1925, **47**, 2340). Similarly, in methyl alcohol a high yield of the bromomethoxy-compound may be obtained (Jackson, *ibid.*, 1926, **48**, 2166). It appears that the extent to which solvent-ion attachment may take place is a function of the rate of the reaction. In acetic acid solution, bromine only is added in the slow reactions, but with the very rapidly reacting undecenoic acid, as much as 30% of the bromoacetoxy-derivative is formed.

Further evidence that the attack is initiated by a positive bromine atom is furnished by the behaviour of ions containing an ethylenic linkage. The allyl group in neutral molecules adds bromine rapidly, but in a positive ammonium ion it is unreactive. On the other hand, acids such as mesaconic and acrylic in aqueous solution have their rate of bromine addition very largely reduced in the presence of a strong acid, which represses the ionisation, and the mesaconate ion reacts 10^4 times as rapidly as the undissociated acid.

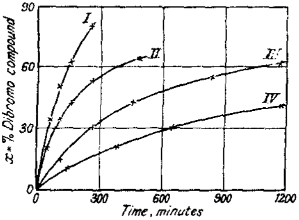
The conclusion of earlier workers that bromine addition is kinetically bimolecular is founded on insufficient evidence: most of the velocities were measured at one concentration only, and even when the initial concentrations were varied (Meyer and Pukall, *Z. physikal. Chem.*, 1929, **145**, 360), no comment was made on the fact that the rate was a function of the concentration. Furthermore, the variation of the bimolecular values of k in a single reaction

has often been considerable. It is now shown that there are three main possibilities: (*a*) unimolecular surface reactions due to impacts of bromine molecules, with rising or falling k_2 (bimolecular coefficient) values according to the conditions, (*b*) homogeneous termolecular reactions, (*c*) homogeneous bimolecular reactions with catalysts but obscured by various disturbing influences.

Reactions in Acetic Acid.—In bromine additions in acetic acid, heterogeneous effects have not been observed, and these reactions are perfectly reproducible and have invariably a positive temperature coefficient; this is unusually small, but this fact is in general accord with the termolecular nature of these processes, which, although unexpected because the reactions are stoicheiometrically bimolecular, has been established as a result of the following considerations. First, the k_2 values fall as the reaction proceeds (x is the % absorption of bromine, and the solutions were $M/40$):

x, %	20	30	40	50	60	70
Allyl acetate, k_2 (25°)	28	25	22	20	18	14
cis-Cinnamic acid, k_2 (25°)	0·13	0·12	0·10	0·087	0·067	0·054

Correspondingly, the values of k_2 at different dilutions for the same fraction of change are different, and calculation of the order of the reaction shows that $n = 3$. To determine the relative participation of the reacting molecules, experiments were carried out in which the proportions of bromine and of ethylenic compound were severally doubled, and it was found that the rate was greater when the bromine was in excess (see figure), showing that two molecules of bromine participate for each molecule of ethylenic compound.



I, $Br_2\ \frac{M}{40}$, A $\frac{M}{40}$; II, $Br_2\ \frac{M}{40}$, A $\frac{M}{80}$; III, $Br_2\ \frac{M}{80}$, A $\frac{M}{40}$; IV, $Br_2\ \frac{M}{80}$, A $\frac{M}{80}$.

Kinetic considerations indicate that the ratio of times for the formation of equal amounts of the dibromophenylpropionic acid should be initially 3 : 1; actually the value as read from the curve at $x = 30\%$ is 3·2 : 1.

With the reactants present in equimolecular amounts (a), so that the relative proportions remain constant throughout the reaction, it is in effect the same whether each molecule of bromine contributes one atom or whether the added bromine atoms are derived from a single molecule, so that:

$$dx/dt = k_3\,(a - x)\,(\tfrac{1}{2}a - \tfrac{1}{2}x)\,(\tfrac{1}{2}a - \tfrac{1}{2}x)$$

and

$$k_3 = (2/t)\,[1/(a - x)^2 - 1/a^2]$$

With this formula satisfactory termolecular constants are obtained. The following values are for *cis*-cinnamic acid at 25°.

x, %	20	30	40	50	60
k_3 ($M/40$)	22	23	22	22	19
k_3 ($M/80$)	21	20	20	21	20

In Table I are collected the average k_3 values of various compounds in acetic acid solution at concentrations of $M/20$—$M/80$.

TABLE I.

	Allyl acetate.	Allyl chloro-acetate.	Allyl benzoate.	Allyl phenyl-acetate.	*cis*-Cinnamic acid.
$k_3 \times 10^{-2}$ (25°)	48·5	21	42·5	45·5	0·21
$k_3 \times 10^{-2}$ (50°)	69	26	70·5	73	0·47
E, calc.	2700	1600	3900	3600	5800

For the determination of the critical increment of these reactions, the temperature range over which measurements can be made is limited on one hand by the freezing point of the

solvent, and on the other, by the fact that at higher temperatures bromine attacks the acetic acid. Accordingly, observations were made at only two temperatures, 25° and 50°, the relatively small changes in the values of k_3 justifying this somewhat extended range. In accord with the general expectation for a termolecular reaction at the ordinary temperature, the critical increments are small. In applying the formula, rate $= P \, . \, Z_3 \, . \, e^{-E/RT}$, where Z_3 is the number of termolecular collisions, it is to be noted that the expression for Z_3 (Steiner, *Z. physikal. Chem.*, 1932, *B*, **15**, 249) contains a doubtful term, *viz.*, the time during which the three molecules are within molecular distance. Further, Gerschinowitz and Eyring (*J. Amer. Chem. Soc.*, 1935, **57**, 985) point out that the rotation of the molecules and their internal degrees of freedom must be taken into account as well as the number of collisions. Approximate evaluations for the present reactions indicate that P is of the order unity, *i.e.*, the majority of the termolecular impacts would seem to be effective, at all events in the region $M/40$. At lower concentrations, as is seen by the trend of n from 3 towards 2, the reaction tends to become bimolecular. Ashdown (*ibid.*, 1930, **52**, 268) found that the reaction between butyl alcohol and *p*-nitrobenzoyl chloride was termolecular (two molecules of alcohol to one of acid chloride), with a somewhat higher value of k_3 at infinite dilution.

Certain compounds, however, appear to give bimolecular constants; *e.g.*, for *trans*-cinnamic acid :

x, %	20	30	40	50
k_2 ($M/40$)	0·035	0·035	0·035	0·035
k_2 ($M/80$)	0·017	0·017	0·016	0·016

but the variation of the velocity constant with the initial concentration, yielding here a value $n = 3{\cdot}1$, indicates that these reactions are, like those just considered, also termolecular. For some compounds, *e.g.*, *trans*-croton-*p*-bromoanilide, k_2 even rises as the reaction proceeds :

x, %	20	30	40	50	60
k_2 ($M/40$)	0·18	0·22	0·27	0·32	0·38
k_2 ($M/80$)	0·10	0·13	0·17	0·21	0·26

It is found that the compounds which do not show falling values of k_2 have the *trans*-configuration, and their behaviour is caused by stereo-conversion during the reaction. The observed velocity of bromine addition is then dependent on (*a*) the rate of the *trans*- ⟶ *cis*-change, (*b*) the rate of addition to the *trans*-form, (*c*) the rate of addition to the *cis*-form. Hydrogen bromide accelerates (*a*), and cinnamic acid, for example, with added hydrogen bromide, has its rate increased to that of the *cis*-isomer.

Reactions in Carbon Tetrachloride.—A marked characteristic of bromine additions in this solvent is the occurrence of certain irregularities, which have been attributed in general to heterogeneous effects, to considerable variations in rate under apparently identical conditions (Sudborough, J., 1910, **97**, 715), to a negative temperature effect (Davis, *J. Amer. Chem. Soc.*, 1928, **50**, 2770), or to a relatively very rapid initial rate of reaction (Herz and Mylius, *Ber.*, 1906, **39**, 3816; Linstead, J., 1927, 356). It is now further established that packing with glass beads may accelerate the reaction very considerably. In certain slow reactions a period of induction has been observed (Williams and James, J., 1928, 343); but this is not necessarily a heterogeneous effect, for it is now found with compounds such as vinyl bromide and acrylic acid in acetic acid solution, where heterogeneous disturbances are absent.

The compounds especially examined in carbon tetrachloride in the present investigation are certain allyl esters and undecenoic acid. At 25° at a concentration of $M/40$, allyl acetate and chloroacetate give rising k_2 values, which are somewhat less at 0°. At 50°, however, there is a very considerable decrease in rate, and the k_2 values now fall as the reaction proceeds (see Table II).

TABLE II.

	Allyl acetate in CCl_4.			Allyl chloroacetate in CCl_4.		
x, %.	k_2 (0°).	k_2 (25°).	k_2 (50°).	k_2 (0°).	k_2 (25°).	k_2 (50°).
20	1·4	0·70	0·078	0·35	0·28	0·025
60	2·3	1·5	0·050	0·50	0·42	0·016

The rising k_2 values at 0° and 25° indicate a unimolecular reaction due to collisions of bromine molecules on a surface film of unsaturated compound, the film being re-formed as fast as it is depleted. At 50° this film is no longer stable, and the reaction now is homogeneous and is actually termolecular in character (as it is in acetic acid solution). This conclusion with regard to the existence of a reactive surface film is confirmed by the results obtained on keeping the bromine concentration constant, and altering that of the unsaturated compound; *e.g.*, doubling the concentration of allyl acetate gives a fictitious bimolecular value, which is smaller in magnitude; in reality the reaction is to be interpreted as being unimolecular with regard to the bromine, and the k_1 value increases from 0·018 to 0·022, the increase being small because the surface film is already almost saturated. Reducing the allyl acetate concentration to one-half causes a very considerable drop in the rate, as the concentration is now not great enough to cause the formation of a stable film.

This interpretation is in accord with the results obtained for equimolecular proportions at different concentrations:

	$M/20$.	$M/40$.	$M/80$.	$M/160$.
Allyl acetate (k_2)	3·0	0·70	0·014	—
Allyl chloroacetate (k_2)	1·4	0·28	0·008	0·003

The concentration range $M/40$—$M/80$ represents for these compounds a region below which the surface film tends to become unstable. In this region, under apparently identical experimental conditions, the heterogeneous reaction may or may not occur. This is illustrated by reference to allyl chloroacetate at $M/40$. In addition to four values in the vicinity of $k_2 = 0·28$, a fifth was obtained widely different, *viz.*, $k_2 = 0·017$, the heterogeneous reaction apparently not having developed in this case.

It is further to be noted with reference to the values in the foregoing table that, whereas at $M/40$ the k_2 values rise as the reaction proceeds, yet at $M/20$ k_2 falls. At this higher concentration the surface film is depleted more rapidly than it is re-formed, and this effect is generally found in the rapid heterogeneous reactions, being previously reported as a rapid initial rate of reaction.

Undecenoic acid produces a more stable surface film which persists at as low a concentration as $M/320$. Correspondingly, this compound exhibits a small negative temperature coefficient from 25° to 50°, indicating that even at 50° the heterogeneous reaction is proceeding.

The fact that an ethylenic compound may combine with bromine at a slow termolecular rate, or undergo under modified conditions a rapid heterogeneous change, gives an explanation of the differences observed for ethylene itself in its reaction with bromine in carbon tetrachloride. Whereas Davis (*loc. cit.*) found a low and decreasing k_2 value, D. M. Williams (J., 1932, 2911), as may be calculated from his curves, observed a velocity 50 times as great. It is further to be noted that, with falling temperature, G. Williams (J., 1932, 1747) found in the gas reaction $C_2H_4 + Br_2$ an increase in velocity and a change from a bi- to a unimolecular reaction.

The general conclusion with regard to the rapid reactions in carbon tetrachloride is that they are largely due to bimolecular impacts on an activated surface film, the formation of which is a consequence of the low internal pressure of the solvent (which determines the fugacity of the solute, *i.e.*, its predilection for a second phase). It appears that the attachment of the ethenoid molecules in the surface film renders them in some way more active, for they are susceptible to bimolecular impacts, whereas in solution termolecular collisions are required for chemical change. It is possible that such surface effects occur in other reactions, but usually they are not detected since the homogeneous reactions are also bimolecular. In bromine addition the heterogeneous effect is especially noticeable, as the homogeneous reaction, being termolecular, is relatively slow.

The Influence of Hydrogen Bromide.—In the reaction $C_2H_4 + Br_2$, hydrogen bromide is non-catalytic in the gas phase (G. Williams, *loc. cit.*) and also in dry carbon tetrachloride solution (Davis, *loc. cit.*). In wet carbon tetrachloride, on the other hand, it acts as a powerful catalyst for this reaction (D. M. Williams, *loc. cit.*). Similar results were obtained by Williams and James (*loc. cit.*) for a number of ethylenic compounds in this solvent.

The influence of hydrogen bromide on the rate of addition of bromine in acetic acid solu-

tion has been examined by D. M. Williams (J., 1932, 979) for cinnamic acid. Although the effect here is very much smaller than in carbon tetrachloride, it is attributed to the same cause. A re-examination of this reaction, as well as that of the *cis*-isomer, gave the following results :

Cinnamic acids in acetic acid (M/80) (25°).

		k_2 (*trans*).			k_2 (*cis*).			
x, %.	[HBr]/[Br_2] 0.	⅛.	¼.	0.	⅛.	¼.	½.
20	0·017	0·067	0·068	0·065	0·065	0·067	0·067
50	0·016	0·046	0·045	0·038	0·046	0·049	0·050

It is evident that hydrogen bromide is not a catalyst for the *cis*-acid, and its effect on cinnamic acid is to convert it into the *cis*-isomer, which reacts as such. Allyl acetate was likewise examined in acetic acid, and hydrogen bromide found to be non-catalytic. As, however, some hydrogen bromide is produced in the course of the reaction, the rate was redetermined in the presence of lead acetate, which converts the hydrogen bromide into insoluble lead bromide. Here also for the four allyl esters no alteration in rate was observed during the early stages of the reaction, and after 50% change the lead acetate had a positive effect.

Two compounds have been discovered, however, *viz.*, vinyl bromide and acrylic acid, which differ in a marked degree from *cis*-cinnamic acid and allyl acetate. In the first place these compounds exhibit extended periods of induction, even in an ionising solvent such as acetic acid. Secondly, they are extremely sensitive to mere traces of hydrogen bromide, and in acetic acid solution give rising k_2 values, in all probability owing to the production of small amounts of hydrogen bromide. The reaction between bromine and acrylic acid was examined with various amounts of hydrogen bromide; the results (Table III) were perfectly reproducible and gave no evidence of heterogeneous disturbances.

TABLE III.

Acrylic acid in acetic acid (25°) ; *values of* k_2 (M/80).

x, %.	[HBr]/[Br_2] $\frac{1}{20}$.	⅛.	¼.	½.	1.	2.	3.	4.	5.
20	—	—	0·26	0·33	0·50	0·57	0·46	0·40	0·40
30	0·035	0·14	0·25	0·31	0·48	0·57	0·43	0·38	0·34
40	—	0·14	0·25	0·32	0·49	0·53	0·41	0·37	0·33
50	—	0·14	0·24	0·33	0·44	0·49	0·39	0·35	0·32
60	—	0·14	0·24	0·32	—	0·44	—	0·31	—
70	—	0·14	0·22	0·31	—	0·41	—	0·23	—

This reaction is very sensitive to added water, which reduces the rate; *e.g.*, for [HBr]/[Br_2] = ½ :

H_2O, %	0·15	0·50	1·0	3·0
k_2	0·32	0·11	0·051	0·050

The maximum velocity shown with increasing amounts of hydrogen bromide in pure acetic acid is due to two opposing tendencies : (i) its catalytic influence, and (ii) the removal of bromine as HBr_3, which appears to be inactive. With the smaller amounts of hydrogen bromide the k_2 values are approximately constant during the reaction, but this is accidental, being the result of the same two opposing tendencies. As the proportion of hydrogen bromide increases, this equalising effect no longer operates, and k_2 falls as the reaction proceeds. Finally, by doubling and halving the relative proportions of acrylic acid (when [HBr]/[Br_2] = ½), and keeping the concentration of bromine unaltered, identical k_2 values were obtained. The conclusion is that the reaction is truly bimolecular, and that the hydrogen bromide activates the bromine and not the ethylenic compound.

It is apparent, then, that bimolecular impacts of HBr_3 and ethylenic compounds must be ineffective, just as they are in substitution reactions, *e.g.*, acetaldehyde and bromine in water (Bugarszky, *Z. physikal. Chem.*, 1901, **38**, 561). In the termolecular reactions in the presence of hydrogen bromide there must likewise be a considerable proportion of HBr_3 present ([Br_2][HBr]/[HBr_3] = 0·006; Jones, J., 1911, **99**, 402). It would seem, therefore, as hydrogen bromide does not alter the rate, that collisions between the ethylenic compound

and two bromine molecules, or two HBr_3 molecules, or one of each, are all approximately equally effective. Such termolecular collisions must also be assumed for acrylic acid, but they must be relatively very much less numerous than the effective bimolecular impacts, and do not perceptibly influence the rate. No explanation is at present offered to account for this difference between cinnamic and acrylic acids, which appears even more marked when the rates in the presence of water are added for comparison :

	HOAc.	HOAc + HBr.	HOAc + 25% H_2O.
Acrylic acid (*M*/80, 25°), k_2	0·005	0·3	0·2
cis-Cinnamic acid (*M*/80, 25°), k_2	0·07	0·07	140

Vinyl bromide behaves similarly to acrylic acid, and of the compounds examined these are the only two that readily polymerise, but there is no evidence of polymerisation as a side reaction.

The influence of hydrogen bromide on bromine-addition reactions has also been studied in carbon tetrachloride. The values in Table IV were obtained for allyl chloroacetate.

TABLE IV.

Allyl chloroacetate in CCl_4 (k_2 *values at* 25°) *with various amounts of* HBr.

		M/40.			*M*/80.				*M*/160.	
x, %.	[HBr]/[Br_2]	$\frac{1}{6}$.	$\frac{1}{3}$.	$\frac{2}{3}$.	$\frac{1}{3}$.	$\frac{2}{3}$.	2.	4.	2.	4.
10		11	18	44	6	11	59	18	13	18
20		7	18	20	4	7	33	17	8	13
30		5	14	13	3	5	21	14	7	10
40		4	10	10	3	4	16	10	6	9
50		4	8	7	3	4	12	8	5	8
60		3	7	6	2	3	9	7	4	8
70		3	6	5	—	3	8	6	—	7

The same rise to a maximum velocity with increasing hydrogen bromide concentration as was found for acrylic acid in acetic acid solution is again observed here and is attributed to the same cause, *viz.*, HBr_3 formation. But here the k_2 values fall very rapidly as the reaction proceeds. This cannot be due to removal of bromine as HBr_3 to a relatively greater extent in the later stages of the reaction, since, for acrylic acid under the same conditions, the k_2 values are constant or decrease only slightly. In carbon tetrachloride the reactions are in part heterogeneous, and accordingly, where the reaction is most rapid there is the greatest fall in k_2 value; the surface films are depleted more rapidly than they can be regenerated. Further evidence is that the reactions are more rapid at 0°; with acrylic acid in acetic acid, where the reaction is homogeneous, there is a normal positive temperature effect.

The Influence of Water.—In the reaction between ethylene and bromine in the gas phase, it was found that water had an accelerating influence and changed the order from 2 to 1 (G. Williams, *loc. cit.*). In carbon tetrachloride, drying tends to reduce the rate of the reaction, according to earlier work. The interpretation is that water causes the formation of reactive surface films. In the present experiments the condition of drying was such that added water had merely a slight accelerating effect on existing heterogeneous reactions.

The catalytic influence of water on the addition of bromine to cinnamic acid was shown in acetic acid solution by D. M. Williams (*loc. cit.*), and it is now found for other compounds. Under certain conditions, however, water may even act as a negative catalyst, as in the reaction between bromine and acrylic acid in the presence of hydrogen bromide. Williams's theory that hypobromous acid is the active catalyst is improbable, as it is proved experimentally that the rate of the change, $Br_2 + H_2O \rightarrow HBr + HBrO$, in acetic acid solution is very slow (see p. 342). An explanation can be found, however, from general kinetic considerations. The effect of water on the rate of bromine addition to *cis*-cinnamic acid is to change the order from 3 to 2, whilst at the same time the value of E rises. Normally the effect of catalysts is to decrease the energy of activation, but here another mechanism is in operation. The order of the reaction has been reduced in the presence of water, thereby increasing the rate by more frequent collisions of the reactants to an extent which is not

offset by the increased energy of activation. This would seem to be a type of catalysis not hitherto reported. The influence of water is shown in Tables V and VI.

TABLE V.

cis-*Cinnamic acid in* HOAc; *influence of water* (25°).

x, %	20	30	40	50	60
k_2 (H_2O 10%, N/10-H_2SO_4), M/80	11·1	9·3	8·3	7·1	5·4
k_2 (H_2O 10%, N/10-H_2SO_4), M/160	6·9	6·1	5·4	5·0	—
k_2 (H_2O 25%, N/4-H_2SO_4), M/80	67	68	63	56	50
k_2 (H_2O 25%, N/4-H_2SO_4), M/160	67	68	64	57	51
k_2 (H_2O 25%), M/80	—	138	115	103	—

With 10% of water (with addition of sulphuric acid to repress ionisation) there is a partial change to a bimolecular reaction ($n = 2·5$); with 25% of water, the identity of the k_2 values at the two concentrations indicates $n = 2$, although there is still a downward trend of k_2. This is attributed to the formation of HBr_3 from hydrogen bromide produced with the greater water content. This fall in the k_2 values makes the determination of E somewhat uncertain; from measurements at 0° for the first part of the reaction, values of 8,500 at M/80 and 8,500 at M/160 were obtained (in acetic acid, $E = 5,800$). A set of k_2 values obtained in the absence of sulphuric acid is included to show the effect of the acid in retarding the rate by its removal of the rapidly reacting cinnamate ions.

TABLE VI.

Acrylic acid in acetic acid and water (25°).

H_2O, %	25.	50.	100.		100 (+N/10-H_2SO_4).	
x, %.	k_2 (M/80).	k_2 (M/80).	k_2 (M/80).	k_2 (M/160).	k_2 (M/80).	k_2 (M/160).
20	0·21	3·2	240	400	—	34
30	0·19	2·9	190	290	34	32
40	0·19	2·8	250	250	29	29
50	0·18	2·1	130	200	25	25
60	0·16	1·3	100	200	23	23

The k_2 values in water show by their downward trend the influence of the hydrogen bromide formed in (*a*) reducing ionisation, and (*b*) forming unreactive HBr_3; the rate in water is greater at M/160 owing to greater ionisation. The N/10-sulphuric acid represses the ionisation, and the identical k_2 values at each concentration indicate the bimolecular nature of the reaction, although there is still a downward trend of k_2 owing to HBr_3 formation.

In water, bromine addition becomes very rapid, and when the reactants are acids the rates are still further increased by formation of the more reactive anions. To determine the rate of reaction of this ion, *e.g.*, in sodium acrylate, it is necessary to remove the hydrogen bromide formed in the course of the reaction, and this was effected by addition of excess of sodium acetate; sodium acrylate (M/500) then gave the following values:

x, %	30	40	50	60	70
k_2 (25°)	8600	8900	8600	9000	9300

It is finally to be noted that these bimolcular reactions in aqueous acetic acid and water are insensitive to light.

EXPERIMENTAL.

The bromine was distilled over potassium bromide, and the middle fraction collected. The acetic acid was purified by Orton and Bradfield's method (J., 1927, 983) and found by f. p. to contain 0·12—0·18% of water, which could be removed only with difficulty. This acid is referred to as acetic acid, and special experiments showed that 0·05% of water (or 0·5% of acetic anhydride) had little effect on the rate; the values in each table are for the same sample of acetic acid. The carbon tetrachloride was washed with dilute potassium dichromate and acid, then dilute sodium hydroxide, and finally with water, left over anhydrous sodium sulphate, refluxed with phosphoric oxide, and finally fractionated; b. p. 76·5°/760 mm. For the very rapid reactions,

special rapid-delivery pipettes were used, and times measured with a stop-watch to half seconds. Either the reaction vessel was broken in a bottle containing potassium iodide solution, or a stream of concentrated iodide solution was blown rapidly into the liquid. For the slower reactions, a small brown-glass bottle was used, which was initially nearly filled with the reaction mixture so as to leave a relatively small air space above the solution; portions were withdrawn by a pipette at the requisite intervals for titration. As the air space above the liquid increases in volume, there is a continual slight loss of bromine by evaporation. Blank tests at 25° with bromine solutions of different concentrations, from which portions were removed at intervals, revealed that under the experimental conditions this loss did not become appreciable until 80% of the bromine was absorbed. At 50° this loss was appreciable at $x = 50\%$, and at this temperature the determinations were carried out in sealed tubes, or small stoppered vessels opened only once.

The values of x were plotted against the time, and from the resultant smoothed curves, the values of k were calculated in g.-mol./l.-min. The results for the reactions described as homogeneous are perfectly reproducible, and were frequently checked by separate observers. The heterogeneous reactions, on the other hand, are not perfectly reproducible, but when an adjustment is made graphically for the short inhibition periods that frequently occur, the variations in the rate are inconsiderable.

A source of error in the heterogeneous reactions is due to the change in the ratio of volume to surface as portions are removed from the reaction vessel. It was estimated that under the experimental conditions this variation over the range $x = 10$—60% would be of the order 20%. No correction is applied, and such a variation is small in comparison with the changes in rate at different temperatures and concentrations.

When the ethylenic compound and bromine are present in equivalent proportion, the k_2 values are presented, even when the reactions are not bimolecular, as they offer a convenient means of comparing the nature of the velocity changes occurring with alterations in temperature or concentration. Unless otherwise specified, all the k_2 values quoted in the text are for $x = 20\%$.

The following compounds have been used in the investigation: allyl acetate, b. p. 103·5—104·5°/760 mm., from allyl alcohol and acetic acid; allyl chloroacetate, b. p. 162—163·5°/766 mm., from allyl alcohol and chloroacetyl chloride; allyl benzoate, b. p. 226—227°/748 mm., from allyl alcohol and benzoyl chloride; allyl phenylacetate, b. p. 239—240·5°/761 mm., from allyl alcohol and phenylacetyl chloride; cinnamic acid, m. p. 134°; *cis*-cinnamic acid, m. p. 68°, from phenylpropiolic acid; cinnamo-*p*-chloroanilide, m. p. 182°, from cinnamyl chloride and *p*-chloroaniline; cinnamo-*p*-bromoanilide, m. p. 192°, cinnamo-2 : 5-dichloroanilide, m. p. 174°, crotono-*p*-chloroanilide, m. p. 169°, all similarly prepared; crotonic acid, m. p. 72°; acrylic acid, b. p. 138·5—139·5°/760 mm.; undecenoic acid, m. p. 24°.

The experimental results are largely quoted in the course of the discussion. In addition to these compounds there were also examined the following: allyl benzoate and phenylacetate in carbon tetrachloride; in general, the results were similar to those obtained for allyl acetate, although the heterogeneous effects here were less marked. This is indicated by the following comparative figures:

	Acetate.	Chloroacetate.	Phenylacetate.	Benzoate.
k_2 (CCl_4, 0°)	1·4	0·35	0·057	0·013
k_2 (HOAc, 25°)	28	15	28	26

Undecenoic acid showed in acetic acid solution a very rapid termolecular rate with a small heat of activation ($E = ca.$ 3000 cals.), as for the other termolecular reactions. In carbon tetrachloride, it gave heterogeneous reactions even at 50°: k_2 (M/320, 25°) = 1·6; k_2 (M/320, 50°) = 0·73.

Cinnamo- and crotono-*p*-bromo (and chloro) anilides were also examined in acetic acid, and gave results corresponding with those obtained for cinnamic acid.

Vinyl bromide in acetic acid was similar in its behaviour to acrylic acid, giving a marked period of induction, and being sensitive to hydrogen bromide.

D. M. Williams's theory (see p. 340) that the catalytic activity of water in bromine addition is due to the formation of hypobromous acid was tested by examining the equilibrium, $Br_2 + H_2O \rightleftarrows HBr + HBrO$, in acetic acid solution. A solution containing 5% of water and lead acetate, and saturated with lead bromide at 25°, was found to be sensitive to added hydrogen bromide (deposit of lead bromide) in a concentration of M/2000. On the other hand, when bromine vapour was added until the concentration reached M/40, and the solution was kept in the dark at 25° and examined at intervals, only after 4 days (duplicate experiments) had a faint deposit of

lead bromide become perceptible. The amount of hypobromous acid formed in the relatively short half-reaction times of the reactions investigated must therefore be very small.

We are indebted to Messrs. M. B. Rands and T. A. Rafter for permission to include reference to certain of their experimental results.

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70. *The Displacement of Bromine from Mono- and Di-bromoethylbenzenes.*

By William Taylor.

Halogen may be displaced from alkyl halides dissolved in dry or wet alcohol or wet acetone in three ways. Two of these are substitution reactions which have been discussed by Gleave, Hughes, and Ingold (J., 1935, 237), one being apparently unimolecular and the other bimolecular. The third, also bimolecular, consists in the elimination of hydrogen halide, resulting in olefin formation (Olivier, *Rec. trav. chim.*, 1934, **53**, 1093; Hughes, *J. Amer. Chem. Soc.*, 1935, **57**, 708; Taylor, J., 1935, 1514; Hughes, Ingold, and Shapiro, J., 1936, 225; see also *Chem. and Ind.*, 1936, **55**, 275, 312, 383, 422). Recently Hughes, Ingold, and Scott (*Nature*, 1936, **138**, 120) have found that a unimolecular olefin reaction operates in sulphur dioxide, and this constitutes a fourth way by which halogen may be displaced from alkyl halides in solution. It is possible that the thermal dissociation of such compounds (no solvent being present), which commonly results in olefin elimination, resembles the fourth method.

In the present investigation the displacement of bromine from four of the five (side-chain brominated) mono- and di-bromoethylbenzenes in dry and in aqueous ethyl alcohol was studied. The fifth, ββ-dibromoethylbenzene, could not be prepared sufficiently pure for kinetic purposes from phenylacetaldehyde, and one attempt to obtain it from benzylmagnesium bromide and bromoform yielded dibenzyl instead. The results for the four compounds can be briefly stated: (1) the unimolecular olefin reaction was never observed; (2) αα-dibromoethylbenzene underwent the unimolecular substitution reaction only; and (3) the other three compounds suffered bromine displacement by all the first three methods, resembling *iso*propyl bromide in this respect (Hughes, Ingold, and Shapiro, *loc. cit.*). However, except αα-dibromoethylbenzene, only α-bromoethylbenzene displayed any large proportion of the unimolecular displacement. The nature and proportions of the products formed are shown in Table I, and the kinetic details of the two bimolecular processes in Table II.

The values of the first-order velocity coefficient for α-bromoethylbenzene in dry ethyl alcohol, constant over approximately the first 50% of change, then show a downward drift. The alcoholysis of the whole molecule, judged by the acidity of the solution, is never completed, and it might appear that the system is reversible. However, after a relatively long time, there is actually a considerable decrease in the acidity of the solution, and this at least cannot be due to the reversibility of the system. Similar observations on the decrease in acidity are true also for αα-dibromoethylbenzene in dry ethyl alcohol. Ward (J., 1927, 2285) found by a titration method that benzhydryl chloride, dissolved in ethyl alcohol, suffered a unimolecular displacement of chlorine. Norris and Morton (*J. Amer. Chem. Soc.*, 1928, **50**, 1795), using a conductance method, concluded that the reaction was reversible, *i.e.*:

$$CPh_2HCl + EtOH\ (excess) \rightleftharpoons CHPh_2{\cdot}OEt + HCl.$$

It is probable that the apparent reversibility was due to esterification of the dry ethyl alcohol (water greatly retards such esterification; cf. Hinshelwood, J., 1935, 599) by hydrogen halide (see, however, Kny-Jones and Ward, *J. Amer. Chem. Soc.*, 1935, **57**, 2394). That is the explanation now offered for these two systems in which hydrogen bromide is liberated, since it was discovered that the rate of disappearance of hydrogen

TABLE I.

Products from the bimolecular reactions in dry ethyl alcohol, with [KOH or NaOEt] ~ 0·2.

(No olefin was formed in dry alcohol alone, at 55° or 25°.)

Compound.	Olefinic product.	Substitution product.	Olefin, %, at 25°.	55°.
1. $Ph\cdot CBr_2Me$	None	Acetophenone diethylacetal	0	0
2. $Ph\cdot CBrH\cdot CH_2Br$	α-Bromostyrene	β-Bromo-α-phenyldiethyl ether (?)	86·6	86·5 ± 1·4
3. $Ph\cdot CBrHMe$	Styrene	α-Phenyldiethyl ether	19·3	20·7 ± 0·6
4. $Ph\cdot CH_2\cdot CH_2Br$	Styrene	β-Phenyldiethyl ether	91·1	91·9 ± 1·2

TABLE II.

Details of the above bimolecular processes.

[KOH or NaOEt] ~ 0·2; k_2 is expressed as g.-mol./l./sec.; $\sigma_{A,B} = 5 \times 10^{-8}$ cm.

Compound.	Reaction.	E (cals.).	$PZ \times 10^{-12}$.	$k_2 \times 10^4$. Obs.	Calc.	P.
$Ph\cdot CBrH\cdot CH_2Br$	Both	16,850	10·2	450	84·7	5·3
$Ph\cdot CBrH\cdot CH_3$	Substitution	22,400	1·70	0·618	0·00719	86*
	Olefin	22,600	1·46	0·385	0·00521	74*
$Ph\cdot CH_2\cdot CH_2Br$	Substitution	21,600	0·0495	0·185	0·0739	2·5
	Olefin	21,000	1·47	1·90	0·0256	74

* These values are only approximate because of uncertainty regarding the values of E (see p. 349).

bromide in initially dry ethyl alcohol was, for all practical purposes, unaffected by the presence of α-phenyldiethyl ether or acetophenone diethylacetal, the "immediate" end-products of the two reactions.

The possibility of a minute but actual reversibility under the given experimental conditions still remains.

Under suitable experimental conditions alcohols and ethers react with hydrogen halides to give alkyl halides, and it has been found (Bennett and Reynolds, J., 1935, **134**, for alcohols and hydrogen bromide; Hinshelwood, *loc. cit.*, for methyl and *tert.*-butyl alcohols and hydrogen chloride; Ghaswalla and Donnan, J., 1936, **1341**, for phenolic ethers and hydrogen halides) that these reactions may be represented as proceeding in two stages: (*a*) the formation of a complex and (*b*) the elimination of R·OH, where R = aryl radical or hydrogen, *i.e.*, ROAlk + HX ⟶ ROAlk,HX ⟶ AlkX + ROH. Reverse processes, such as the unimolecular hydrolysis or alcoholysis of alkyl halides, may reasonably be supposed to follow the reverse path and both stages might, under favourable conditions, be "slow." The first stage would be pseudo-unimolecular because of the huge excess of the solvent ROH, and the second would also be unimolecular, so making the whole process kinetically of the first order and the rate proportional to the concentration of the alkyl halide, which coincides with experimental results. Evidence of the formation and decomposition of such a complex in the reverse processes is found in the high values of P shown in Table III, where the activation energy (Arrhenius) has been increased by Q' of the equation $-d\log_e\eta/dT = Q'/RT^2$, and the calculated velocity coefficient has been obtained from $k = Be^{-E/RT}$, where $B = 3\pi N\eta\sigma(M_A + M_S)/2M_AM_S$ (Glasstone, "Recent Advances in General Chemistry," 1936, 292). These high values are comparable with those calculated in a similar manner from the observations of von Halban (*Ber.*, 1908, **41**, 2417; *Z. physikal. Chem.*, 1909, **67**, 129), Fletcher and Hinshelwood (J., 1935, 596), and Hinshelwood (*loc. cit.*) on the unimolecular decompositions of phenylbenzylmethylallylammonium bromide, triethylsulphonium bromide, diphenyliodonium bromide, and the presumed methoxonium chloride respectively. In the light of these results, it is probable that the value of $P{\sim}1$ for the hydrolysis of substituted benzyl halides in aqueous ethyl alcohol (50%), calculated by Moelwyn-Hughes ("The Kinetics of Reactions in Solution," 1933, p. 161) from the work of Olivier (*Rec. trav. chim.*, 1922, **41**, 301, 646; 1923, **42**, 516, 775), is due to the instability of the complex, so that the second stage is rapid. The increase in the velocity of such unimolecular reactions of alkyl halides brought about by partially substituting water for alcohol as the solvent (see Table III) is in keeping with the mechanism now proposed, since

Bennett and Reynolds, Hinshelwood, and Ghaswalla and Donnan (*locc. cit.*) have noted the retarding effect of water on the direct reaction, and hence this solvent would, on this scheme, be expected to facilitate the reverse reaction. The present intermediate "complex" hypothesis for the unimolecular substitution reaction of alkyl halides is distinct from the "ionisation" mechanism of Gleave, Hughes, and Ingold (*loc. cit.*) since the *direct* intervention of the solvent in the rate-determining stages of the reaction is here postulated.

TABLE III.

Details of the unimolecular process in dry and in aqueous alcohol.

(Q' has been calculated from Intl. Crit. Tables; σ is the geometric mean diameter of the solute molecule; k_1 is expressed as sec.$^{-1}$.)

Compound.	EtOH, % by vol.	Temp.	$\sigma \times 10^8$, cm.	E, cals.	Q', cals.	E, corr.	$PZ \times 10^{-14}$.	$k_1 \times 10^5$, obs.	$k_1 \times 10^6$, calc.	$P \times 10^3$.
CHBrPhMe	100	25°	6·1	21,640	3,480	25,120	0·185	0·685	1·92	0·357
	80	25	6·1	21,670	4,520	26,190	25·5	15·4	0·552	27·8
CHClPhMe *	80	25	5·9	21,380	4,520	25,900	0·996	1·00 †	0·931	1·07
$CHMe_2Br$ ‡	80	50	5·2	23,160	4,320	27,480	0·0561	0·134	1·12	0·120
	60	50	5·2	22,690	4,910	27,600	0·202	0·411	1·24	0·333
CMe_3Cl §	80	25	5·9	23,060	4,520	27,580	11·5	0·914	0·0605	15·1
	50	25	5·9	22,920	5,450	28,370	1780	36·6	0·0255	1960
CBr_2PhMe	100	25	7·2	22,580	3,480	26,060	7·65	5·68	0·436	13·3
	80	25	7·2	18,620	4,520	23,140	1·96	211	110	1·92
CCl_2PhMe	100	25	6·7	24,120	3,480	27,600	9·32	0·525	0·0324	16·2

* From Ward (J., 1927, 445).
† Value obtained by extrapolation.
‡ From Hughes, Ingold, and Shapiro (*loc. cit.*).
§ From Hughes (J., 1935, 255).

EXPERIMENTAL.

Preparation of Materials.—α-Bromoethylbenzene (15 g.) was prepared by the method of Ashworth and Burkhardt (J., 1928, 1791) from styrene (10 g.) and a cold solution of dry hydrogen bromide (27 g.) in glacial acetic acid (50 c.c.); b. p. 105°/30 mm. (Found: Br, 43·5. Calc.: Br, 43·2%). It was also obtained by passing (2 hrs.) dry hydrogen bromide through styrene (18 g.) cooled in carbon dioxide–ether. No trace of purple colour developed (contrast the preparation of αα-dibromoethylbenzene); excess hydrogen bromide was promptly removed by dry carbon dioxide (½ hr.). Distillation gave two fractions: (1) b. p. 104°/26 mm. (3·5 g.), (2) b. p. 94°/14 mm. (28 g.), which was α-bromoethylbenzene. This was hermetically sealed in small glass tubes, for exposure to air soon caused cloudiness. In this preparation all hydrogen bromide must be promptly removed before distillation, for in an experiment in which it was not completely removed, the pressure during distillation was not sufficiently reduced for some 3 hours, during which the temperature was 180°; two fractions of equal bulk were then obtained: (1) b. p. 100—101°/20 mm. (α-bromoethylbenzene); (2) b. p. 185—190°/15 mm., a colourless oil with a blue fluorescence which slowly disappeared. The latter was presumably "liquid distyrene," since Erlenmeyer (*Annalen*, 1865, **135**, 122) obtained it by heating styrene for many hours with hydrochloric acid (*d* 1·12) at 170°, and it had b. p. 310° at ordinary pressure.

β-Bromoethylbenzene, prepared by refluxing β-phenylethyl alcohol with constant-boiling hydrobromic acid, had b. p. 105—106°/18 mm. (Found: Br, 43·0. Calc.: Br, 43·2%).

The preparation of αα-dibromoethylbenzene presented difficulties (see this vol., p. 304). The addition of phenylacetylene (8 g.) to an ice-cold solution of dry hydrogen bromide (27 g.) in glacial acetic acid (50 c.c.) produced after 3 days acetophenone (1·5 g.), styrene dibromide (0·2 g.), and dypnone (4·5 g.) (oxime, m. p. and mixed m. p. 131—133°). When, however, dry hydrogen bromide was passed for 2 hours through phenylacetylene (20 g.) cooled in carbon dioxide–ether, a deep purple colour developed, which disappeared on removal of the excess of hydrogen bromide by dry carbon dioxide, and on distillation three fractions were obtained: (1) b. p. 70—100°/15 mm. (22 g.), (2) b. p. 100—115°/11 mm. (5 g.), (3) b. p. 116—118°/10 mm. (16 g.). Fractions (1) and (2) had the odour of α-bromostyrene. Fraction (3) was the αα-dibromoethylbenzene used in the kinetic experiments (although α-bromostyrene was present as an impurity, this difficulty was immaterial, for the effect of its presence was always examined). It was a pale yellow, fairly pungent-smelling liquid, which fumed slightly in air and became cloudy within 1 minute; therefore it was immediately sealed in glass tubes (Found: Br, 56·4. Calc.: Br, 60·6%). A further amount was obtained by passing dry hydrogen bromide for

1 hour through fraction (1) surrounded by ice–salt, the same procedure as above then being followed. No purple colour developed. Two fractions were collected: (1*a*) b. p. 100—118°/15 mm. (13 g.), (1*b*) b. p. 118—120°/15 mm. (7 g.); (1*b*) contained Br, 60·0% and was similar in properties to (3). The αα-dibromoethylbenzene was identified by keeping a solution of fraction (3) (*ca.* 3 g.) in alcohol (70 c.c.) and water (30 c.c.) at 55° for 16 hours and then refluxing it for 1 hour with semicarbazide hydrochloride (1·5 g.) and sodium acetate (5 g.); acetophenone semicarbazone (1·7 g.) was obtained, m. p. 196° (after recrystallisation from alcohol) and mixed m. p. 196—197°. The b. p. of the liquid precluded it from containing much, if any, styrene dibromide, which, according to Anschütz (*Annalen*, 1886, **235**, 328), has b. p. 139—141°/15 mm., and kinetic experiments showed that none of this isomer was present.

αα-Dichloroethylbenzene was prepared in a similar manner by adding dry hydrogen chloride to phenylacetylene (3 g.); the mixture became purple and finally deep green and a colourless liquid (4·5 g.) was obtained (Found: Cl, 35·6. Calc.: Cl, 40·6%). This liquid, which fumed in air and became cloudy within a few minutes, was hermetically sealed; after a day or so it became bright green and then brown. Its identity was established by the preparation (from 2·5 g.) of acetophenonesemicarbazone (2·2 g.), m. p. 195° after recrystallisation from alcohol.

αβ-Dibromoethylbenzene, obtained by Glaser's method (*Annalen*, 1870, **154**, 154), had m. p. 73°. Acetophenone diethylacetal was prepared by Claisen's method (*Ber.*, 1907, **40**, 3908).

Products of Reactions of α-Bromoethylbenzene.—(a) *With ethyl alcohol.* α-Bromoethylbenzene (4 g.), dissolved in dry ethyl alcohol (100 c.c.), was kept at 55° for 16 hrs. A slight excess of solid potassium carbonate was added to neutralise the liberated hydrogen bromide, the alcohol distilled off, dry ether added, and the potassium bromide filtered off. Only α-phenyldiethyl ether, b. p. 69—71°/13 mm., was obtained (Found: OEt, 29·0. Calc.: OEt, 30·0%). Quantitative analysis of the product for styrene (see p. 347) showed that it was absent.

(b) *With* 80% *ethyl alcohol.* A mixture of alcohol (80 c.c.), water (20 c.c.), and α-bromoethylbenzene (5 g.) was treated as in (a), except that after addition of potassium carbonate (to remove water), the mixture was filtered; on distillation, a colourless liquid (1·6 g.), b. p. 66—88°/10 mm., was obtained. This contained no styrene (bromine did not give styrene dibromide) and from the b. p. range was presumably a mixture of α-phenyldiethyl ether and phenylmethylcarbinol; Ward (J., 1927, 452) found that α-chloroethylbenzene and 80% alcohol at 50° yielded this mixture.

(c) *With alcoholic potash.* A solution of α-bromoethylbenzene (6·5 g.) in dry ethyl alcohol (300 c.c.) and alcoholic potash (30 c.c.; approx. 2*N*) was maintained at 55° for 4 hours. The liquid was added to water (1 l.); this was extracted with ether, from which were obtained two fractions: (1) b. p. 35—74°/15 mm. (1·2 g.), (2) b. p. 74—76°/15 mm. (2·9 g.). Fraction (1) was dissolved in an equal bulk of chloroform, and bromine added drop by drop; styrene dibromide (0·35 g.) was obtained. Fraction (2) was mainly α-phenyldiethyl ether but contained 7·4% of styrene as found by the method on p. 347.

(d) *With alcoholic sodium ethoxide.* A solution of α-bromoethylbenzene (3 g.) in the reagent (50 c.c., approx. *N*), kept at 55° for 17 hours, gave a liquid of b. p. 30—40°/12 mm., which with bromine yielded styrene dibromide and was mainly styrene. In this case the reaction liquid was much more strongly alkaline than in (c).

Products of Reaction of Alcoholic Potash with β-Bromoethylbenzene.—A solution of β-bromoethylbenzene (6 g.) in dry alcohol (300 c.c.) and alcoholic potash (30 c.c.; approx. 2*N*) was maintained at 55° for 20 hours, and then worked up as in (c), above, giving two fractions: (1) b. p. 44—46°/17 mm. (3·0 g.); (2) b. p. 88—90°/15 mm. (0·4 g.). Fraction (1) was styrene (Biltz, *Annalen*, 1897, **296**, 274, gives b. p. 43°/17 mm.). Fraction (2) was mainly β-phenyldiethyl ether (Found: OEt, 27·6. Calc.: OEt, 30·0%); 0·216 g. of (2) also gave styrene dibromide (0·035 g.). Ashworth and Burkhardt (*loc. cit.*) found styrene as the only product, but the concentration of their alcoholic potash was not stated.

Products of Reactions of αα-Dibromoethylbenzene.—(a) *With ethyl alcohol.* A solution of αα-dibromoethylbenzene (1·4 g.) (Found: Br, 56·4%) in dry alcohol (10 c.c.) was kept at 55° for 1½ hours; distillation afforded, after removal of the alcohol, (1) a liquid of b. p. 80—94°/11 mm. (0·6 g.) (Found: Br, 32·2; OEt, 4·6%), and (2) a white crystalline solid (0·15 g.) (Found: Br, nil), m. p. 170°, very sparingly soluble in alcohol. It is probable that (1) was a mixture consisting mainly of α-bromostyrene, present as impurity in the original αα-dibromoethylbenzene, and some acetophenone diethylacetal (Arbusow, *Ber.*, 1907, **40**, 3303, gave b. p. 103·5—104°/17 mm. for the latter). The solid (2) was *s*-triphenylbenzene (Engler and Dengler, *Ber.*, 1893, **26**, 1445, gave m. p. 169—170°). Claisen (*Ber.*, 1898, **31**, 1020) showed that acetyl chloride reacts vigorously with acetophenone diethylacetal to give *s*-triphenylbenzene, so pre-

sumably this compound is obtained here by the interaction of hydrogen bromide on the acetal in *dry* alcohol.

(b) *With* 80% *alcohol.* αα-Dibromoethylbenzene (0·31 g.) (Found : Br, 56·0. Calc. : Br, 60·6%) in dry alcohol (8 c.c.) and water (2 c.c.) were kept at 55° for 74 hours, then neutralised with sodium hydroxide and heated at 55° with a slight excess of semicarbazide acetate (½ hr.). Acetophenonesemicarbazone (0·06 g.) was obtained.

(c) *With potassium hydroxide and* 80% *ethyl alcohol.* αα-Dibromoethylbenzene (0·24 g.) (Found : Br, 56·0%) in dry alcohol (7 c.c.), alcoholic potash (1 c.c., approx. 2*N*), and water (2 c.c.) were similarly treated, hydrochloric acid being used for neutralisation; 0·04 g. of semicarbazone was obtained. This and the previous experiment indicate the formation of approximately the same proportion of acetophenone with or without alkali in 80% alcohol.

(d) *With alcoholic sodium ethoxide.* αα-Dibromoethylbenzene (4 g.) (Found : Br, 49·0%) in dry alcohol (200 c.c.) containing excess of the ethoxide was heated at 55° for 30 mins., then added to water (500 c.c.) and extracted with ether. A colourless liquid (2 g.), with the odour of acetophenone diethylacetal and of b. p. 90—95°/11 mm., was obtained (Found : Br, 21·0; OEt, 10·0%), but no *s*-triphenylbenzene. The liquid (0·44 g.), refluxed with semicarbazide hydrochloride (0·5 g.) and sodium acetate (0·5 g.) in alcohol (30 c.c.) and water (5 c.c.) for 1 hr., gave no acetophenonesemicarbazone, but an oil. When, however, 1·0 g. was refluxed with a slight excess of semicarbazide hydrochloride in alcohol (30 c.c.) and water (5 c.c.) for 15 mins., followed by heating with sodium acetate for 1 hour, acetophenonesemicarbazone (0·60 g.) was obtained. The liquid was thus a mixture of α-bromostyrene and acetophenone diethylacetal. α-Bromostyrene (0·7 g.), from styrene dibromide, treated in exactly the same way, gave no semicarbazone, but an oil. Hence the semicarbazone derived from the αα-dibromoethylbenzene product is not formed from the α-bromostyrene present as impurity.

Although experiments (a) and (d) do not exclude the possibility of the formation of α-bromostyrene from αα-dibromoethylbenzene, the olefin estimations (p. 348) show conclusively that this compound is not formed either with or without sodium ethoxide in dry alcohol.

Products of Reaction of Alcoholic Potash with αβ-Dibromoethylbenzene.—αβ-Dibromoethylbenzene (5 g.) in dry alcohol (200 c.c.) and alcoholic potash (20 c.c.; approx. 2*N*) were warmed at 55° for 10 mins., then poured into water (1 l.) and extracted with ether. A liquid (2·5 g.), b. p. 105—110°/37 mm., 81—86°/9 mm., was obtained (Found : Br, 43·0. Calc. for α-bromostyrene : Br, 43·7%. Calc. for β-bromo-α-phenyldiethyl ether : Br, 34·5%). Ashworth and Burkhardt (*loc. cit.*) found only α-bromostyrene in this reaction. They accounted for Nef's obtaining phenylpropiolic acid on treatment of the product with sodium and carbon dioxide (*Annalen*, 1899, **308**, 273) as being due to the presence of unchanged αβ-dibromoethylbenzene : Nef held that it was due to the presence of β-bromostyrene. From the bromine content, but more particularly from the results of olefin determination (see Table I), it appears probable that β-bromo-α-phenyldiethyl ether is formed, along with α-bromostyrene, in this reaction.

Estimation of Olefin.—Styrene and α-bromostyrene, products from the mono- and one of the di-bromoethylbenzenes respectively, were estimated by bromine addition. The results are given in Table I. There were two difficulties : (1) the rapid bromine substitution of the ethyl ethers (and especially of α-phenyldiethyl ether), also present with the olefins, even at room temperature in daylight, and (2) the slow rate of addition of bromine to α-bromostyrene. The following are the details of a control experiment for the estimation of a relatively small amount of styrene in presence of α-phenyldiethyl ether. To styrene (0·0170 g.; 1·64 × 10^{-4} g.-mol.) and α-phenyldiethyl ether (0·1522 g.; 10·15 × 10^{-4} g.-mol.), dissolved in carbon tetrachloride (20 c.c., 99·9%) in a stoppered bottle fitted with an opaque covering and cooled in ice–salt, was added dropwise and with shaking, standard bromine (AnalaR) in carbon tetrachloride (99·9%). The liquid, still in ice–salt, was left in the dark for 30 mins., treated with excess potassium iodide, and then titrated with sodium thiosulphate. The result showed a quantitative addition of bromine to the styrene, and a similar result was obtained when styrene (0·0209 g.) was mixed with α-phenyldiethyl ether (0·1567 g.). In estimating α-bromostyrene, owing to the marked effect of temperature on the rate of addition of bromine, duplicate experiments were performed on the products from the same reaction liquid over different time intervals at room temperature. Consistent results were accepted as a true measure of the amount of α-bromostyrene.

The following procedure for extraction and estimation of the products from the reaction of α- and β-bromo- and αβ-dibromo-ethylbenzenes was therefore adopted, after control experiments had shown that the method gave quantitative results for styrene. A solution of the compound under investigation, in dry alcohol (10 c.c.) either with or without sodium ethoxide or potassium hydroxide, the reactants being of concentrations similar to those used in kinetic experiments,

was maintained at 55° or 25° for a slightly longer time than had been found necessary for the elimination of one bromine atom. The liquid was then added to water (100 c.c.), and twice extracted with carbon tetrachloride (10 c.c. and 5 c.c.). The total extract was washed with water (50 c.c.) and run into a stoppered bottle, this water being finally extracted with a further 5 c.c. of tetrachloride and the extract run into the bottle. In all cases the procedure from this point was exactly as for the control experiment on styrene, except that for bromine addition to the products from αβ-dibromoethylbenzene the time was 3—7 days and the temperature that of the room.

The estimation of possible α-bromostyrene formation from αα-dibromoethylbenzene required separate treatment. The compound as prepared was always associated with α-bromostyrene, and further, acetophenone diethylacetal in the products suffers ready acid hydrolysis to acetophenone (cf. Haworth and Lapworth, J., 1922, **121**, 76) which is easily brominated. The procedure was to extract the products of reaction in dry alcohol, either with or without sodium ethoxide, after elimination of two bromine atoms, exactly as with the other three compounds. The tetrachloride extract (20 c.c.) was shaken at room temperature with *N*/10-hydrochloric acid (25 c.c.) for 30 mins. and then with a saturated sodium bisulphite solution (50 c.c.) for 15 mins. After separation, the aqueous layer was extracted with more solvent (5 c.c.) and the 25 c.c. of tetrachloride were washed with two successive amounts of 50 c.c. of water. Each of these two aqueous liquids was extracted with carbon tetrachloride (5 c.c. each) and the extracts washed. The bromine addition to the resulting extract (35 c.c.) was effected exactly as for the products from αβ-dibromoethylbenzene. From the amount of α-bromostyrene found and that of αα-dibromoethylbenzene used, as estimated by acid or alkali titration, the bromine content of such a mixture was calculated, and it was always in very close agreement with that of the original mixture. Hence, no α-bromostyrene was formed during the reaction of αα-dibromoethylbenzene in dry alcohol, either with or without sodium ethoxide. For example, with αα-dibromoethylbenzene (Found: Br, 53·5%): (*a*) 10 c.c. of dry alcoholic solution after 30 mins. at 55° gave a titre of 6·60 c.c. of *N*/10-sodium hydroxide, representing αα-dibromoethylbenzene, and finally after bromine addition a difference in titre of 6·95 c.c. of *N*/10-sodium thiosulphate, representing α-bromostyrene, which would mean a bromine content of 53·4% for the supposed mixture; (*b*) 10 c.c. of dry alcoholic solution with [NaOEt] = 0·1260 after 30 mins. at 55° gave a titre of 6·53 c.c. of *N*/10-hydrochloric acid, *i.e.*, 6·07 c.c. represent αα-dibromoethylbenzene, and finally after bromine addition a difference in titre of 6·05 c.c. of *N*/10-thiosulphate, representing α-bromostyrene, which would mean a bromine content of 53·6% for the supposed mixture.

Kinetic Experiments.

The ethyl alcohol throughout was dried as described (Taylor, *loc. cit.*). In each experiment, 100 c.c. of a solution of the bromo-compound either in dry alcohol with or without potassium hydroxide or sodium ethoxide, or in aqueous alcohol (80% by vol.) with or without potassium hydroxide at the required temperature were taken. In the bimolecular reactions between potassium hydroxide or sodium ethoxide and β-bromo- or αβ-dibromo-ethylbenzenes, where the unimolecular mechanism was negligible, the reaction was stopped by adding 10 c.c. of the reaction liquid to about 50 c.c. of cold water. In all other cases this addition was to benzene (25 c.c.) and water (50 c.c.). The resulting liquid was titrated with *N*/10-aqueous acid or alkali (phenolphthalein).

The equations $k_1 = (2\cdot303/t) \,.\, \log_{10}a/(a-x)$ and $k_2 = [2\cdot303/t(a-b)] \,.\, \log_{10}b(a-x)/a(b-x)$, where t is the time in mins. (unless otherwise stated), and a and b are respectively the concentrations of bromo-compound and potassium hydroxide or sodium ethoxide in g.-mols./l., were used in calculating the velocity constants for the uni- and the bi-molecular reactions respectively.

α-Bromoethylbenzene.—In dry alcohol alone the earlier values of k_1 for a unimolecular reaction are reasonably constant, but later, esterification of the solvent by the liberated hydrogen bromide causes first a decrease in the values of k_1 and then decrease in acidity, as the following details of an experiment at 55° show.

Expt. 2. $a = 0\cdot1020$.

t.	NaOH, c.c.	k_1.	t.	NaOH, c.c.	k_1.	t.	NaOH, c.c.	k_1.	t.	NaOH, c.c.	k_1.
4·85	0·57	0·0119	37·8	3·60	0·0115	114	7·25	0·0109	293	9·10	0·0076
10·9	1·18	0·0113	62·2	5·22	0·0115	178	8·55	0·0102	1267	7·30	—
21·7	2·27	0·0116	71·5	5·55	0·0110						

In dry alcohol containing sodium ethoxide all three reactions operate, as is indicated by an

increase in the value of the first-order velocity "constant" ($\mathbf{k}_1$) over that in dry alcohol alone, and by a gradual fall in the values of $\mathbf{k}_1$ and a gradual rise in $\mathbf{k}_2$ during any one run. Thus the displacement of halogen from this compound resembles the corresponding displacement from *iso*propyl bromide (Hughes, Ingold, and Shapiro, *loc. cit.*). Using their notation and their method of calculation of the total second-order constant k_2, for an experiment at 55°, we get (see Table IV): mean total $k_2 = 0{\cdot}158$ when [NaOEt] $= 0{\cdot}1622$.

TABLE IV.

Expt. 3. $a = 0{\cdot}0760$; $b = 0{\cdot}1622$; $k_1 = 0{\cdot}01165$.

t.	HCl, c.c.	$\mathbf{k}_1$.	$\mathbf{k}_2$.	$k_1/(b-x)$.	$t \cdot d\mathbf{k}_2/dt$.	Total k_2.
0	16·22	—	—	—	—	—
4·65	15·18	0·0316	0·202	0·0763	0·0170	0·143
10·65	14·05	0·0316	0·210	0·0826	0·0160	0·145
20·9	12·55	0·0316	0·224	0·0924	0·0293	0·161
35·0	11·28	0·0307	0·228	0·1028	0·0350	0·160
52·0	10·16	0·0307	0·252	0·1142	0·0350	0·173
73·8	9·44	0·0302	0·265	0·1240	0·0295	0·171
96	9·10	0·0288	0·264	0·1275	0·0192	0·155
198	8·74	—	—	—	—	—
242	8·72	—	—	—	—	—
5565	8·62	—	—	—	—	—

The value of k_2 increases (see Table V) with increasing dilution of the sodium ethoxide, as would be expected if the ethoxide ion is the actual reagent in both the bimolecular reactions, since its activity coefficient will increase with dilution. The fraction of α-bromoethylbenzene destroyed by the unimolecular reaction has been calculated by the method employed by these three authors. The figures for the velocity constants for the two bimolecular reactions—k_2 (olefin) and k_2 (substitution)—are based on the observed percentages of olefin formation given in Table I and on the calculated fraction of the whole reaction which is due to the unimolecular reaction. In view of the facts that for any one temperature this fraction appears to depend, not only on the concentration of alkali, but also upon the relative concentrations of alkali and bromo-compound, and that the concentrations used were similar to, but not identical with, those for olefin estimation, these figures can only be regarded as approximate.

TABLE V.

Summary of the values of velocity constants in dry ethyl alcohol, with and without sodium ethoxide, and of the percentage of α-bromoethylbenzene destroyed by the unimolecular reaction.

(k_1 is expressed as min.$^{-1}$, and k_2 as g.-mol./l./min.)

Expt.	a.	b.	$10^3\,\mathbf{k}_1$.	$10^3\,\mathbf{k}_2$.	$10^3\,k_1$.	$10^3\,k_2$.	Unimolecular reaction (%).	$10^3\,k_2$ (olefin).	$10^3\,k_2$ (substn.).
				Temp. 55°.					
1.	0·0728	—	—	—	11·7	—	—	—	—
2.	0·1020	—	—	—	11·6	—	—	—	—
3.	0·0760	0·1622	31·6—28·8	202—264	(11·65)	158	39·0	54	104
4.	0·0515	0·0800	24·5—22·9	330—489	(11·65)	237	48·6	96	141
5.	0·0732	0·2167 *	47·4—38·9	—	—	—	—	—	—
				Temp. 25°.					
6.	0·1680	—	—	—	0·410	—	—	—	—
7.	0·0774	—	—	—	0·412	—	—	—	—
8.	0·1213	0·1430	1·12—0·95	8·35—11·1	(0·411)	5·49	50·2	2·13	3·36
9.	0·0327	0·0817	0·942—0·938	11·9—12·6	(0·411)	6·55	49·3	2·49	4·06

* Potassium hydroxide was used in this expt.

When aqueous alcohol (80%) replaced the dry solvent, values of the first-order velocity coefficient k_1 were constant throughout the whole of the displacement, whether potassium hydroxide was present or not. The value of k_1 was the same in both cases, and evidently the use of this solvent medium produced a change from a mixed uni- and bi-molecular reaction to one which was entirely unimolecular. The results are summarised below.

Summary of results in aqueous alcohol (80%).

Expt.	Temp.	a.	b.	k_1.	Expt.	Temp.	a.	b.	k_1.
10	55°	0·0737	—	0·263	12	25°	0·2180	—	0·00925
11	55	0·0746	0·2145	0·264					

β-Bromoethylbenzene.—In dry alcohol alone there was no measurable bromine displacement during 24 hrs., but in aqueous alcohol (80%) a unimolecular reaction took place as shown by the following experiment at 55°, where $a = 0{\cdot}1522$.

t (hrs.)	5·5	51	96	200	
NaOH, c.c.	0·10	0·90	1·50	3·00	
$10^3 k_1$ (hr.$^{-1}$)	1·17	1·20	1·08	1·10	Mean 1·14

With potassium hydroxide in dry alcohol, constant values were obtained for a second-order velocity coefficient; details of one experiment at 55° are given.

$a = 0{\cdot}1090$; $b = 0{\cdot}2470$.

t (mins.)	1·95	4·0	7·05	12·5	17·65	24·0	41·5	77	211
HCl, c.c.	23·03	21·82	20·17	18·30	16·91	15·95	14·57	13·95	13·80
k_2	0·369	0·337	0·347	0·341	0·351	0·358	0·371	0·358	—

Mean 0·353

Table VI shows the complete results for alcoholic potash at different temperatures.

TABLE VI.

Temp.	Solvent.	a.	b.	k_2.	k_2 (olefin).	k_2 (substn.).
55°	EtOH	0·1090	0·2470	0·353	0·323	0·029
55	,,	0·0980	0·1965	0·351	—	—
55	EtOH (80%)	0·0690	0·2110	0·153	—	—
45	EtOH	0·1126	0·2348	0·108	—	—
35	,,	0·1208	0·2365	0·0389	—	—
25	,,	0·0765	0·2099	0·0125	0·0114	0·0011

The values of k_2 (olefin) and k_2 (substitution) are computed from the olefin percentages given in Table I.

αα-Dibromoethylbenzene.—This preparation always contained α-bromostyrene, from which alkali caused slow displacement of bromine; further, the hydrogen bromide produced by its alcoholysis was removed (though slowly) by dry alcohol. For these two reasons, the reaction concentration produced by a known weight of αα-dibromoethylbenzene (from any one preparation) in dry alcohol was computed (1) by reference to the hydrolysis of a known weight in aqueous alcohol (80%), and (2) checked by its bromine content (Robertson, J., 1915, **107**, 902). To indicate the variation in the values of the first-order velocity coefficient, details of two runs, both in dry alcohol at 55°, are given (Table VII), one without and the other with sodium ethoxide. The values of k_1 are calculated from the usual equation for a unimolecular reaction (p. 348), x being taken as half the titre (NaOH) or half the difference in titre (HCl); *i.e.*, it is assumed that the two bromine atoms are displaced simultaneously.

TABLE VII.

$a = 0{\cdot}0305$.						$a = 0{\cdot}0245$; $b = 0{\cdot}1620$.					
t.	NaOH, c.c.	k_1.	t.	NaOH, c.c.	k_1.	t.	HCl, c.c.	k_1.	t.	HCl, c.c.	k_1.
1·55	0·96	0·111	30·9	5·90	0·116	0·55	15·92	0·107	32·8	11·48	0·101
3·05	1·74	0·110	63	6·05	—	1·85	15·32	0·107	248	11·28	—
7·0	3·08	0·107	147	5·90	—	4·45	14·20	0·118	119 (hr.)	9·03	—
10·9	4·35	0·115	46 (hr.)	4·61	—	8·53	13·05	0·106	188 (hr.)	8·15	—
18·1	5·30	0·112	282 (hr.)	2·10	—	16·25	12·00	0·112			
Mean $k_1 = 0{\cdot}112$.						Mean $k_1 = 0{\cdot}109$.					

Evidently the only process operating here is unimolecular, and the reaction is not sensitive to alkali. The complete results are given in Table VIII and show that, as usual for this type of unimolecular halogen displacement, water produces a marked increase in the value of k_1. In view of this, the value of k_1 obtained from Expt. 5, in which potassium hydroxide in dry alcohol was substituted for the sodium ethoxide used in other experiments, is interesting since it indicates that in such a solution the equilibrium KOH + dry EtOH (solvent) $\rightleftharpoons$ KOEt + H_2O lies far over to the right. Expt. 5 (Table V) supports this observation, as also does the work of Williams and Bost (*J. Chem. Physics*, *1936*, **4**, *251*).

Two experiments with αα-dichloroethylbenzene and sodium ethoxide in dry alcohol were performed for purposes of comparison with the bromo-compound:

Temp.	a.	b.	k_1.	Temp.	a.	b.	k_1.
55°	0·0260	0·0610	0·0131	25°	0·0370	0·0800	0·000315

TABLE VIII.

Solvent, dry EtOH; [NaOEt] = b; k_1 in min.$^{-1}$.

Expt.	a.	b.	k_1.	Expt.	a.	b.	k_1.
	Temp. 55°.				Temp. 25°.		
1	0·0305	—	0·112	6	0·0315	—	0·00338
2	0·0245	0·1620	0·109	7	0·0274	0·0812	0·00344
3	0·0420	0·1620	0·117	8	0·0455	0·1430	0·00341
4	0·0320	0·0806	0·111				
5	0·0340	0·2080 *	0·152				
	Solvent, aqueous EtOH (80%).						
	Temp. 55°.				Temp. 25°.		
9	0·0903	—	2·19	11	0·0755	—	0·126
10	0·0460	0·1735 *	2·31	12	0·0705	0·1760 *	0·127

* [KOH] = b.

αβ-Dibromoethylbenzene.—Details of the unimolecular displacement in aqueous alcohol (80%) at 55° follow; a = 0·0695.

t (hrs.)	5	28	51	96	218	
NaOH, c.c.	0·65	2·90	4·52	5·85	6·95	
$10^2 k_1$ (hr.$^{-1}$)	1·97	1·89	2·06	1·92	—	Mean 0·0196

In dry alcohol at 55° (a = 0·0878), the mean value of k_1 was 0·000471 hr.$^{-1}$.

All other experiments were performed with potassium hydroxide in dry alcohol, and under these conditions the values of the second-order coefficient are sensibly constant for any one run, *i.e.*, the unimolecular displacement is negligible. The reaction is so fast at 55° that details are afforded for one experiment at 25° in order to illustrate how the values of k_2 vary during one such run.

a = 0·0926; b = 0·2070.

t	0·6	1·2	1·9	2·6	3·5	5·0	6·6	10·3	197
HCl, c.c.	18·15	16·51	15·20	14·20	13·42	12·50	12·13	11·70	11·58
k_2	2·78	2·89	2·73	2·80	2·77	2·91	2·73	2·55	—
								Mean k_2 = 2·77	

Full results are tabulated below :

Temp.	42°	35°	25°	25°	15°
a	0·0613	0·0629	0·0926	0·0944	0·0944
b	0·2387	0·1960	0·2070	0·1977	0·1991
Total k_2	12·5	6·79	2·77	2·61	1·00

From Table I it is seen that the percentages of olefin formation at 55° and 25° are almost identical, and hence the temperature coefficients and activation energies for the bimolecular olefin and substitution reactions were calculated from the values of " total k_2."

Examination for Reversibility in Dry Alcoholic Solutions of Reactions of α-Bromo- and αα-Dibromo-ethylbenzenes.—Dry hydrogen bromide was passed (½ hr.) into dry alcohol surrounded by ice–salt, and the solution immediately diluted with dry alcohol until it was approx. $N/5$. The solutions (2) and (3) were made as soon as possible afterwards (5 mins.), and all three solutions were placed in the thermostat at 55° and allowed to attain its temperature (15 mins.).

The method of procedure was the general one employed in the other kinetic experiments, *i.e.*, benzene (25 c.c.) and water (50 c.c.) were used in stopping the reaction; the titre is given in c.c. of $N/10$-sodium hydroxide.

t (hrs.)		0	0·25	1·1	5	23	47	96	150
Titre	(1) Control expt.	19·10	19·05	18·85	17·73	11·40	8·08	4·15	3·60
	(2) [CHPh(OEt)Me] = 0·0310	19·05	19·00	18·80	17·68	11·20	7·90	4·05	3·45
	(3) [CPh(OEt)$_2$Me] = 0·0513	18·90	18·85	18·65	17·60	10·95	7·60	3·90	3·40

SUMMARY.

1. The different modes of displacement of bromine from α- and β-bromo- and αα- and αβ-dibromo-ethylbenzenes in dry and in aqueous ethyl alcohol (80%) have been studied.

2. Evidence is adduced to show that the apparent unimolecular displacement is actually composite, and generally includes the formation and decomposition of an intermediate complex.

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71. *The Photo-decomposition of Gaseous Acetone.*

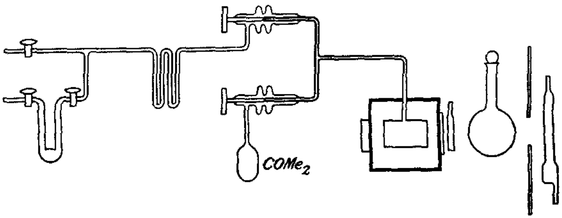
By ROBERT SPENCE and WILLIAM WILD.

IT was shown in an investigation of the photo-decomposition of methyl iodide, alone and in the presence of hydrogen (*Proc. Leeds Phil. Soc.*, 1936, **3**, 141), that the probability of reaction occurring between methyl and hydrogen is less than one in 10^4 collisions at 0°. Further experiments have been carried out with acetone instead of methyl iodide, since acetone is supposed to dissociate in the following manner on absorption of ultra-violet light (Norrish, Crone, and Saltmarsh, J., 1934, 1456): $(CH_3)_2CO + h\nu = 2CH_3 + CO$, and might be expected to yield a higher concentration of methyl than could be obtained from methyl iodide under the same conditions of illumination. According to Norrish *et al.* (*loc. cit.*), the ultimate products of the decomposition of acetone are ethane and carbon monoxide in equal volume. However, our initial experiments in the presence of hydrogen always gave $C_2H_6/CO = 3/2$. Experiments with pure acetone gave the same result, and furthermore, it was found that diacetyl is formed in considerable amount at room temperatures (Spence and Wild, *Nature*, 1936, **138**, 206). A detailed analytical study of the photo-decomposition was therefore undertaken in order to discover the cause of the discrepancy. The analytical results of previous workers are not entirely consistent, and it seems probable that the composition of the products depends largely on the experimental conditions, a conclusion which is fully in agreement with our own experiments.

EXPERIMENTAL.

Acetone (B.D.H. *ex* sodium iodide) was fractionated, and individual samples were dried with calcium chloride, magnesium perchlorate, and phosphoric oxide. Further treatment with

FIG. 1.



sodium iodide and drying agents produced no change in the final results. Acetone thus prepared had the correct b. p. and vapour pressure. The final fractionation was carried out in a vacuum in an all-glass apparatus free from stop-cocks, and the experimental sample was sealed off while frozen in liquid air.

The apparatus was constructed as shown in Fig. 1. A cylindrical quartz reaction vessel, 7 cm. in length and with plane windows 4 cm. in diameter, was connected to the rest of the apparatus by means of a graded seal. It was contained in a substantial aluminium casting to obviate large fluctuations of temperature. The total volume of the reaction system was 77·7 c.c. In order to avoid the effects due to extraneous moisture (Damon and Daniels, *J. Amer. Chem. Soc.*, 1933, **55**, 2365), direct connections to the reaction vessel were made through greaseless Pyrex-glass valves (Bodenstein, *Z. physikal. Chem.*, 1930, *B*, **7**, 387), and this part of the apparatus was separated from the rest, which contained stop-cocks lubricated with Apiezon grease, by a double U-tube cooled in carbon dioxide–acetone or liquid air. Owing to the large number of experiments and the long duration of each, it was necessary to use three different mercury arcs. These were of the straight pattern, working on the 110-volts supply at about 3 amps. The full light of the arc was condensed into an approximately parallel beam by a quartz flask (300 c.c.) filled with water. A photo-electric cell fixed in a suitable position was used as a check on the light intensity. Uncontrollable fluctuations ($\pm 15\%$), probably due to varying line

voltage, occasionally occurred. Using this system, we have been unable to observe any anomalous effects traceable to moisture, nor was there any detectable difference between the samples of acetone subjected to different degrees of drying. The reaction products were pumped off through a liquid-air trap by a Töpler pump, and the non-condensable gases collected and analysed in a special Bone and Wheeler apparatus suitable for small amounts of gas. The general method of analysis was to test first of all for carbon dioxide and oxygen, although these were never present in any measurable quantity. Carbon monoxide was then determined by absorption in ammoniacal cuprous chloride, and the residual gas was exploded with oxygen. After the contraction had been observed, the carbon dioxide produced was absorbed in alkali, thus providing a check on the methane figure calculated from the contraction. In a number of experiments, however, the amount of methane was too small for an accurate combustion determination to be made. A second gaseous fraction, which proved to be pure ethane, was collected with the trap immersed in solid carbon dioxide–ether. Since ethane is readily soluble in acetone (Horiuti, *Sci. Papers Inst. Phys. Chem. Res. Tokyo*, 1931, **17**, 182), the trap was then allowed to warm to room temperature, and again pumped out at $-78°$. This was repeated until no more gas could be obtained. Ethane was determined from the contraction and from the amount of carbon dioxide produced after explosion with oxygen. The ratio C_2H_6/CO remained unchanged when the ethane was collected at $-110°$. Decomposition occurring at room temperatures in the full light of the mercury arc was first studied, an acetone pressure of 160 mm. being used. The results (Table I, *a*) show that the degree of dryness is without appreciable effect on the reaction. The data marked with an asterisk refer to experiments in which the mercury manometer was omitted from the apparatus and in which special care was taken to free the system from extraneous substances. However, the introduction of a mercury manometer did not affect the results. In experiments with 160 mm. of acetone, the fraction of light absorbed would be large.

TABLE I.

Photo-decomposition at Room Temperatures with the Full Arc.

(a) *Influence of drying.*

					Products, c.c. at N.T.P.			$COMe_2$ decomposed.			
No.	Desiccant.	$COMe_2$, mm.	Temp.	Time, hrs.	CO.	CH_4.	C_2H_6.	C.c. at N.T.P.	%.	Yield per 10 hrs.	C_2H_6/CO.
1	$CaCl_2$	160	21·6°	8	1·61	—	2·43	3·25	21·3	4·06	1·51
2	,,	156	19·5	24	4·46	0·22	6·54	8·62	57·9	3·60	1·47
3	$Mg(ClO_4)_2$	164	22·0	14	2·82	—	4·03	5·24	32·8	3·74	1·43
4*	P_2O_5	160	20·0	17	3·39	0·11	4·77	6·14	40·3	3·61	1·41
5*	,,	160	20·0	17	2·72	—	4·18	5·64	36·2	3·34	1·54
6*	,,	160	20·0	17	2·72	—	3·90	5·08	33·3	2·93	1·44
32	$CaCl_2$	160	21·0	17	2·17	0·07	3·29	4·41	28·9	2·60	1·52

(b) *Influence of intensity.*

					Products, c.c. at N.T.P.		$COMe_2$ decomposed.			
No.	$COMe_2$, mm.	Temp.	Time, hrs.	Screen transmission, %.	CO.	C_2H_6.	C.c. at N.T.P.	%.	Yield per 10 hrs.	C_2H_6/CO.
55	163	22·0°	17	100	2·13	3·45	4·77	30·7	2·81	1·62
61	163	19·5	2·5	100	0·29	0·47	0·65	4·2	2·60	1·62
62	164	20·5	3	100	0·428	0·683	0·94	6·0	3·13	1·59
58	162	21·0	19	60	1·07	1·88	2·69	17·4	1·42	1·76
54	165	20·5	15	40	0·566	1·04	1·52	9·7	1·01	1·84
56	161	21·0	24	18	0·399	0·789	1·18	7·7	0·49	1·98
57	161	20·0	48	7	0·313	0·586	0·86	5·6	0·19	1·87
60	164	19·0	67	2·5	0·207	0·323	0·44	2·8	0·066	1·56

The product remaining in the trap was always yellow. The condensate from 20 successive experiments similar to Nos. 4, 5, and 6 (Table I, *a*) was therefore collected in a micro-fractional distillation apparatus, which was sealed to the trap. The latter was subsequently cut off and weighed. A sharp separation of unchanged acetone (0·9 g.) from a yellow liquid (0·1 g.) was achieved by immersing the bulb in a beaker of water, the temperature of which was carefully controlled. It is evident that more acetone entered the reaction vessel than the amount calculated from the pressure (0·78 g.), probably owing to the accumulation of a brown, viscous substance (0·03 g.), extremely soluble in acetone, on the cylindrical wall of the reaction vessel. In later experiments, the reaction vessel was cleaned at frequent intervals. The b. p. (micro-

method) of the yellow liquid was 87—88°, identical with that of pure diacetyl, which was determined simultaneously. The following derivatives were prepared.

Nickel dimethylglyoxime. One drop of the liquid was added to a solution of hydroxylamine hydrochloride (0·5 g.) in water (1 c.c.) and heated to boiling. The white crystalline precipitate was filtered off, washed with cold distilled water, and dried at 100° (cf. Mulliken, "Identification of Organic Compounds," Vol. 1); m. p. 234—236°, showing no depression on admixture with authentic dimethylglyoxime (m. p. 235°). Addition of a few drops of aqueous nickel sulphate to an aqueous-alcoholic solution of the remaining solid gave a scarlet precipitate of nickel dimethylglyoxime.

Diacetyl 2 : 4-dinitrophenylhydrazone. This derivative was prepared by Brady's method (J., 1931, 756). A brown micro-crystalline powder was obtained by recrystallisation from pyridine, and orange leaflets from nitrobenzene, m. p. 336—337°. An authentic sample melted at 337° and the mixed m. p. was the same.

Gas analyses of different experiments in the series gave results similar to those shown in Table I, *a*. Assuming for purposes of calculation, that 3 vols. of ethane are produced for every 2 vols. of carbon monoxide, we can represent the change stoicheiometrically as follows: $4(CH_3)_2CO = 3C_2H_6 + 2CO + (CH_3{\cdot}CO)_2$. The amounts of ethane and carbon monoxide formed would therefore require a yield of 0·105 g. of diacetyl, whereas 0·1 g. was actually obtained. If it is assumed that diacetyl is the sole non-gaseous product, the equation can be written in general form for any C_2H_6/CO ratio, *viz.*,

$$(2y - x)COMe_2 = yC_2H_6 + xCO + (y - x)(COMe)_2 \qquad (1)$$

The number of c.c. of acetone vapour decomposed per 10 hours has been calculated from the yields of ethane and carbon monoxide with the help of the above equation, and the methane which is produced in relatively small amount has been disregarded.

Experiments with Filtered Light.—Having determined the general course of the reaction occurring in the full light of the mercury arc, we carried out experiments in the same apparatus, using filtered light of different intensities.

Filter for the continuum. The quartz flask was filled with a solution of nickel and cobalt sulphates of suitable concentration (Bowen, J., 1935, 76), and used in conjunction with a cylindrical quartz cell (5 cm. × 5 cm.) containing chlorine gas at 420 mm. pressure. Spectrograms taken with a copper-spark source showed that this combination transmitted radiation between 2200 and 2900 A., the greater portion being less than 2750 A. The transmission, which was frequently tested, remained unchanged after long periods of illumination. Different intensities were obtained by interposing calibrated screens of oxidised copper gauze. The results are given in Table II.

TABLE II.

Photo-decomposition in the Region of Continuous Absorption. Influence of light intensity and acetone pressure.

No.	$COMe_2$, mm.	Temp.	Time, hrs.	Screen trans-mission, %.	Products, c.c. at N.T.P. CO.	CH_4.	C_2H_6.	$COMe_2$ decomposed. C.c. at N.T.P.	%.	Yield per 10 hrs.	C_2H_6/CO.
36	160	20·0°	48	100	1·69	0·20	4·13	6·56	43	1·37	2·44
37	160	19·5	21·5	100	0·66	0·06	1·61	2·57	16·9	1·19	2·44
49	161	21·0	17	100	0·63	0·04	1·55	2·48	16·2	1·46	2·47
63	160	20·0	21	60	0·422	—	0·921	1·42	9·3	0·68	2·18
44	160	21·0	25·5	29	0·230	—	0·512	0·794	5·2	0·31	2·23
39	160	20·0	41	12	0·172	—	0·321	0·469	3·1	0·115	1·87
46	160	21·0	48	12	0·169	—	0·275	0·381	2·5	0·079	1·63
40	70	20·0	24	100	0·499	—	0·967	1·44	21·6	0·598	1·94
43	70	20·0	18	100	0·455	—	0·874	1·29	19·4	0·719	1·92
42	32	20·0	26	100	0·427	—	0·690	0·953	31·1	0·367	1·62

The most interesting feature of the experiments with light in the continuum region is associated with the effect of varying intensity. As the light intensity increases from a low value to the highest attainable with the apparatus, the ratio C_2H_6/CO approaches a maximum value of approximately 2·5, as compared with a value of 1·5 for the full arc. Increase of acetone pressure at constant intensity also appears to increase the ratio. Since the continuum light differs from that of the full arc mainly by lack of light in the banded region of absorption, it was thought that the difference in the ratio C_2H_6/CO might be due to a low value in the banded

region. The hypothesis was tested by an experimental determination of the ratio in the band region.

Filters for the band region. The water filter together with a 1 cm. layer of potassium chromate (0·25 g. per litre) transmitted the line 3130 A. and some 3020 A., whilst removing the shorter ultra-violet light and radiation between 3400 and 4360 A. An attempt was made to employ a filter consisting of a 1-cm. layer of potassium phthalate (0·025*M*), but the amount of decomposition obtained was much less than expected, owing to the instability of the filter.

TABLE III.

Photo-decomposition in the Region of Banded Absorption.

					Products, c.c. at N.T.P.		$COMe_2$ decomposed.			
No.	Filter.	$COMe_2$, mm.	Temp.	Time, hrs.	CO.	C_2H_6.	C.c. at N.T.P.	%.	Yield per 10 hrs.	C_2H_6/CO
35	Pyrex	160	19·5°	70·5	0·195	0·173	0·184	1·2	0·026	0·89
53	K_2CrO_4	164	19·5	48	0·283	0·336	0·389	2·5	0·081	1·19
65	,,	164	20·5	46	0·235	0·282	0·325	2·1	0·072	1·20
50	Phthalate	161	20·5	24	0·078	0·078	0·078	0·5	0·033	1·00

Whilst the C_2H_6/CO ratio for the banded region is undoubtedly about unity and much lower than the corresponding ratio for the same rate of decomposition in the continuum, the amount of decomposition is much too small to account for the different values obtained in the full arc and in the region of continuous absorption.

Further experiments with unfiltered light. In order that the conditions governing the value of the ratio C_2H_6/CO might be fully explored, another series of experiments with the full arc was carried out (Table I, *b*). The acetone pressure was maintained constant at 160 mm., and the intensity was systematically reduced by calibrated wire screens of oxidised gauze. The ratio showed a remarkable variation with decrease of light intensity, first increasing to a value of about 2, and then decreasing in the same manner as with the continuum light.

Influence of Temperature on the Photo-decomposition.—Previous investigators (Norrish *et al.*; Damon and Daniels, *locc. cit.*) have usually worked at 60°. We have carefully repeated the experiments at this temperature, using the technique developed by Norrish *et al.* (*loc. cit.*), which appears to be most suitable. Acetone, dried over phosphoric oxide or calcium chloride, was distilled into a quartz bulb (200 c.c.) provided with a side tube, which had been thoroughly baked out in a vacuum. Greased stop-cocks were separated from the apparatus by the folded trap (Fig. 1), during evacuation, after which it was sealed off so that acetone came into contact only with Pyrex glass or quartz during the distillation. When 1 c.c. had collected in the side tube, the bulb was sealed off and placed in a double-walled air-thermostat provided with quartz windows and heated by a stream of air passing through an external heater, as described by Norrish. The wave-length of the light was regulated by filters, and the intensity by wire screens. After illumination, the bulb was removed and attached by rubber pressure-tubing to a U-tube immersed in liquid air, which was connected through a stop-cock to a Töpler pump. The trap was evacuated and allowed to stand for several hours to ensure that no leakage occurred at the rubber connexion, after which the fine capillary seal of the quartz bulb was broken and the gases pumped off. The side limb of the quartz bulb was at first maintained at −78°, and then the acetone was allowed to distil slowly into the trap. A second gaseous fraction was obtained when the temperature of the trap was raised to −110°. It was found later that the gas had the same composition if pumped off at −78°. Analytical results are given in Table IV. The light intensity used by Norrish, as determined from the carbon monoxide yield, was

TABLE IV.

Photo-decomposition at 60°: influence of intensity ($COMe_2$ = 860 mm.).

				Gaseous products.			
No.	Radiation.	Time, hrs.	Screen transmission, %.	C.c. at N.T.P.	CO, %.	C_2H_6, %.	CH_4, %.
24	Full arc	9·5	100	13·52	45·0	41·4	13·6
26	Continuum	24	100	4·15	48·3	33·3	18·4
27	,,	20	100	3·27	47·6	32·6	19·8
30	,,	24	29	1·64	52·6	19·6	27·8
28	,,	15	22	0·73	55·0	18·9	26·0
31	None	24	—	0·00	—	—	—

very similar to that in Expt. 30. The acetone remaining in the trap was always colourless, and no evidence of diacetyl formation at 60° could be obtained.

Owing to the high acetone pressures used in the above experiments (*ca.* 860 mm.), the results cannot be directly compared with those obtained at room temperatures. Accordingly, photolyses were performed at 0° and 51° with acetone pressures of 66 mm. and 80 mm. respectively, so that the fraction of light absorbed should be about the same as in the 70 mm. experiments at room temperatures. Since the vapour pressure at 0° is about 70 mm., higher pressures were precluded. The cylindrical quartz cell previously described was placed in a large, well-lagged, tin box. The end window of the cell was attached by sealing wax to a brass tube 5 cm. long, which passed through the side of the box. A few pieces of silica gel were placed in the tube to prevent the window's becoming fogged, and the cylindrical chlorine filter was waxed to the outer end, thus leaving an air-tight, dry space between the filter and the reaction vessel. The box was filled with an ice-water mixture for the experiments at 0°, and fitted with the usual water-thermostat devices for the experiments at 51°. The results are given in Table V, together with the room-temperature data at 70 mm. pressure for purposes of comparison.

TABLE V.

Influence of Temperature in the Region of Continuous Absorption.

No.	$COMe_2$, *mm.*	*Temp.*	Time, hrs.	Products, c.c. at N.T.P.* CO.	C_2H_6.	$COMe_2$ decomposed. C.c. at N.T.P.	%.	Yield per 10 hrs.	C_2H_6/CO.
67	67·0	0·0°	22	0·265	0·627	0·989	14·4	0·45	2·37
68	66·5	0·0	22	0·230	0·516	0·802	11·7	0·37	2·24
40	70	20	24	0·499	0·967	1·44	21·6	0·60	1·94
43	70	20	18	0·455	0·874	1·29	19·4	0·72	1·92
69	80	51	18	0·540	0·615	0·69	10·0	0·38	1·14
70	83	51	18	0·459	0·495	0·53	7·4	0·30	1·08

* The methane formed in these experiments never constituted more than 5% of the total gaseous products.

The experiments at 0° and 51° were performed after the others, and the same incident intensities could not be obtained. This is reflected in the 10-hour yields. The ratio C_2H_6/CO decreases with rise of temperature, and it is apparent that at 60° no diacetyl can be formed.

DISCUSSION.

The region of the acetone absorption spectrum with which we are concerned, *i.e.*, between 2200 and 3400 A., has been studied by several workers (Norrish, Crone, and Saltmarsh, *loc. cit.*; Bowen and Thompson, *Nature*, 1934, **133**, 571; Norrish, *ibid.*, p. 837; Noyes, Duncan, and Manning, *J. Chem. Physics*, 1934, **2**, 717), and its main features seem to be well established. The long-wave end of the spectrum shows banded structure, which fades at about 3000 A. into apparently continuous absorption extending to 2200 A., whilst the reality of the banded structure is supported by the occurrence of a green fluorescence caused by wave-lengths down to 2800 A. (Norrish, *loc. cit.*; Fisk and Noyes, *J. Chem. Physics*, 1934, **2**, 654). It is probable that the two types of absorption are superimposed over a considerable range, since, according to Howe and Noyes (*J. Amer. Chem. Soc.*, 1936, **58**, 1404), fluorescence can be observed upon excitation by all mercury lines between 3130 and 2536 A.

The quantum yield of the decomposition of acetone at 60° is 0·2 for 3130 A., and 0·4 for 2536 A. (Damon and Daniels; Norrish *et al.*; *locc. cit.*), whereas Leermakers (*J. Amer. Chem. Soc.*, 1934, **56**, 1899) finds that, in the banded region, the quantum yield approaches unity as the temperature is increased to 160° and then remains constant. Norrish (*Trans. Faraday Soc.*, 1934, **30**, 103) has suggested that with simple ketones the primary photochemical process is a dissociation into radicals, and there are now a considerable number of facts with which this theory is consistent; *e.g.*, the photo-decomposition of methyl ethyl ketone yields carbon monoxide and a mixture of ethane, propane, and butane (Norrish and Appleyard, J., 1934, 874), and Pearson (*ibid.*, p. 1718; Pearson and Purcell, J., 1935, 1151) has detected methyl radicals in the products of the photolysis of acetone

by their reaction with metallic mirrors. Furthermore, according to Leermakers (*loc. cit.*), the photosensitisation of the chain decomposition of dimethyl ether is to be ascribed to the production of radicals. However, it has not hitherto been possible to decide which of the following reactions constitutes the primary photochemical process :

$$(a)\ (CH_3)_2CO + h\nu \longrightarrow 2CH_3 + CO - 80 \text{ kg.-cals.}$$
$$(b)\ (CH_3)_2CO + h\nu \longrightarrow CH_3 + CH_3{\cdot}CO - 89{\cdot}5 \text{ kg.-cals.}$$

Norrish has stated with reference to this difficulty, that if equation (*b*) is correct, the acetyl radical must break up spontaneously, since no appreciable quantity of diketone is detectable in the products. Our experiments at 60° are in agreement with this view, but it is evident from the semi-quantitative separation of diacetyl and the value of the C_2H_6/CO ratio at room temperatures that reaction (*b*) is the primary process, and that the acetyl radical is capable of a separate existence. Diacetyl had previously been detected in the products of photo-decomposition at room temperatures by Barak and Style (*Nature*, 1935, **135**, 307), but in the absence of quantitative data it was not then possible to arrive at definite conclusions as to the nature of the primary process.

The non-gaseous product is mainly diacetyl (see p. 354), and it is probable that the residue consists of polymerides with the same empirical formula. The use of equation (1) for the calculation of the amount of acetone decomposed would therefore appear to be legitimate. Fluctuations of the incident light intensity were unavoidable with our apparatus, but inspection of Table I, *b*, where the data for a number of consecutive experiments with the same arc are given, will show that a 40-fold increase in the intensity is accompanied by a 40-fold increase in the hour yield. The linear relation between light intensity and rate of decomposition is not so obvious in the continuum experiments at constant pressure (Table II), because of the fluctuations of the arc. However, if the percentage of incident light absorbed at the three different pressures shown in Table II is calculated with the aid of the absorption coefficients for acetone (Porter and Iddings, *J. Amer. Chem. Soc.*, 1926, **48**, 40), the result is found to be in good agreement with the ratios of the hour yields. The quantum yield is therefore independent of light intensity and of acetone pressure.

Although, in some experiments, the final partial pressure of diacetyl was considerable, no secondary effects due to its presence could be detected. The absorption spectrum of diacetyl covers the same region as that of acetone and extends into the longer wave-lengths as far as the blue, and according to Porter, Ramsperger, and Steel (*ibid.*, 1923, **45**, 1827), it is decomposed by ultra-violet light at 100°, yielding 2 vols. of carbon monoxide and 1 vol. of ethane. Norrish, however, has reported (*Trans. Faraday Soc.*, 1931, **27**, 405) that the gaseous products contain 85% of carbon monoxide. If either of these processes occurred to a measurable extent in our experiments, the ratio C_2H_6/CO would be expected to decrease as the period of illumination increased. No such decrease is apparent, and it is to be inferred that at room temperatures diacetyl vapour possesses considerable stability towards light.

Photo-decomposition in the Continuum Region.—The ratio C_2H_6/CO obtained with light of different intensities in the continuum (Table II) for a constant acetone pressure of 160 mm. is plotted against the rate of decomposition of acetone in Fig. 2. The ratio first increases rapidly with increasing intensity, and then approaches a maximum value of about 2·5. If we write down a probable series of intermediate reactions, *viz.*,

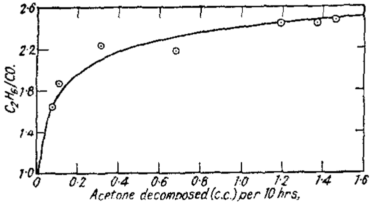
$$(1)\ (CH_3)_2CO + h\nu \longrightarrow CH_3 + CH_3{\cdot}CO \qquad (2)\ 2CH_3 \longrightarrow C_2H_6$$
$$(3)\ 2CH_3{\cdot}CO \longrightarrow (CH_3{\cdot}CO)_2 \qquad (4)\ CH_3 + CH_3{\cdot}CO \longrightarrow C_2H_6 + CO$$
$$(5)\ CH_3{\cdot}CO \longrightarrow CH_3 + CO$$

and suppose that at moderate pressures and intensities the stationary concentrations of methyl and acetyl are about the same, the equation $d[C_2H_6]/d[CO] = 1/(k' + k''/\sqrt{I_{abs.}})$ can be deduced from the rates of formation and removal of the intermediates. Evaluating the constants with the aid of the experimental results and assuming that $d[C_2H_6]/d[CO] = C_2H_6/CO$, we obtain

$$C_2H_6/CO = 1/(0{\cdot}3391 + 0{\cdot}077/\sqrt{I_{abs.}})$$

where $I_{abs.}$ represents the hour yield. This relation is plotted in Fig. 2, the experimental points being shown. At very low intensities, the methyl and the acetyl radical concentrations would be widely different, and the above equation, which tends to zero as $I_{abs.} \longrightarrow 0$, would no longer apply. The ratio approaches a maximum value at high intensities owing to the operation of reaction (4), which cannot be replaced by the recombination reaction $CH_3 + CH_3{\cdot}CO \longrightarrow (CH_3)_2CO$. Reaction (5) is necessary to explain the decrease in C_2H_6/CO at low intensities, and offers the most convenient explanation of the influence of temperature. The relative importance of (5) will increase as the intensity decreases, until ultimately all acetyl radicals will decompose before they can combine by (3) and the ratio will become equal to unity. A secondary generation of acetyl radicals by the reaction $CH_3 + (CH_3)_2CO \longrightarrow C_2H_6 + CH_3{\cdot}CO$ is excluded because it introduces the possibility of chains, and it is known that the quantum yield does not become greater than unity at higher temperatures (Leermakers, *loc. cit.*; Norrish and Akeroyd, J., 1936, 190). When the C_2H_6/CO–hour-yield data for the experiments at 70 mm. and 32 mm. (Table II) are plotted, the points are found to lie considerably below the curve for 160 mm. (Fig. 2), *i.e.*, the ratio decreases with the pressure. This behaviour would be expected if reaction (5) were wholly or partly heterogeneous, since diffusion to the walls would be facilitated by decrease of pressure. Alternatively, if reactions (2) and (3) required the intervention of a third

Fig. 2.



Variation of C_2H_6/CO ratio with rate of photo-decomposition of 160 *mm.* COMe$_2$ *by continuum light.*

molecule, the ratio would again be less at the lower pressures. It appears to be the total pressure which is concerned here, and not simply the acetone pressure, since the ratio in long experiments with about 50% of decomposition (Table II) is the same as in short experiments in which only a small fraction of the acetone is decomposed. The fall in the light absorption would have only a slight effect on the ratio at high intensities (Fig. 2), but if it depended on the partial pressure of acetone, a considerably smaller value would be expected with a large percentage of decomposition. The products of decomposition as well as acetone itself, therefore, either facilitate reactions (2) and (3) or prevent the diffusion of acetyl radicals to the walls.

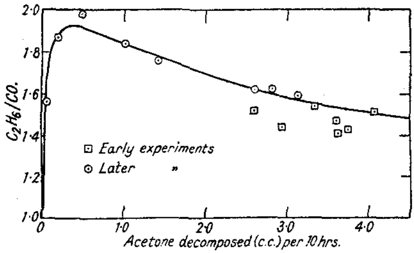
Photo-decomposition in the Banded Region.—A value for the quantum yield in the banded region at room temperatures is given by Leermakers (*loc. cit.*), *viz.*, 0·04, and the very slow rate of decomposition obtained in our experiments (Table III) can only be accounted for if the quantum yield is very much smaller than in the continuum. Moreover, if the values of C_2H_6/CO are plotted against the hour yield, the points will be found to lie well below the continuum curve (Fig. 2). In other words, the low value of the ratio cannot be ascribed to the smallness of the hour yield. Since all radiation below 3130 A. is cut off by the Pyrex plate, and all below 2950 A. by the chromate filter, there would appear to be a photochemical threshold at about 3000 A., on the short-wave side of which the type of decomposition described in Table II occurs, and on the long-wave side of which we have another type in which the ratio C_2H_6/CO is unity. However, a sharply defined threshold is scarcely to be expected because of the overlapping of the banded and continuous absorption to which allusion has already been made. Absorption in the continuum leads

to the production of free radicals, and in these circumstances the ratio C_2H_6/CO must depend on the conditions. On the other hand, if we suppose that light absorption in the banded region yields an excited molecule which is deactivated either by collision or by fluorescence, or which produces ethane and carbon monoxide directly, the experimental result that $C_2H_6/CO = 1$ can be explained. Patat (*Z. physikal. Chem.*, 1934, *B*, **25**, 208; Patat and Löcker, *ibid.*, 1935, *B*, **27**, 431) has suggested that a similar state of affairs exists in the case of formaldehyde. The suggested mechanism for the photo-decomposition in the banded region is therefore :

(6) $(CH_3)_2CO + h\nu \longrightarrow (CH_3)_2CO^*$
(7) $(CH_3)_2CO^* \longrightarrow (CH_3)_2CO$ (deactivation or fluorescence)
(8) $(CH_3)_2CO^* \longrightarrow C_2H_6 + CO$

Norrish has supposed that the primary dissociation into radicals in the continuum necessitates a radiationless transition from an upper excited state to a second unstable state. Essentially the same process is envisaged for the band region, with the exception that the unstable state is different and leads to normal molecules instead of radicals. The fact that Leermakers's experiments in the banded region at higher temperatures appear to

FIG. 3.



Variation of C_2H_6/CO *ratio with rate of photo-decomposition of* 160 *mm.* $COMe_2$ *in the full arc.*

involve radical decomposition does not invalidate the above mechanism. It is possible that, when light in the banded region is absorbed by molecules in high vibrational levels, the probability of transition from the excited state to an unstable state yielding radicals is increased to such an extent that the decomposition into normal molecules becomes negligible. This is rendered probable by that fact that light of wave-length 3130 A. possesses just sufficient energy to effect the decomposition into radicals.

Photo-decomposition in the Full Arc.—The experimental data for different intensities of the full arc (Table I, *a* and *b*) are plotted in Fig. 3. Consideration of the hour yields given in Tables II and III shows that by far the greater part of the decomposition occurring in the full arc is due to the continuum light. The published transmission values of the filters for the band region being used, the maximum diminution in the ratio which can be ascribed to the presence of light in the banded region is 0·2. For higher intensities, the ratio is about 2·5 in the continuum and 1·5 in the full arc. The decomposition occurring in the banded region alone is therefore much too small to account for the difference. However, it is possible that excited acetone molecules produced in this region are particularly efficient in effecting the decomposition of acetyl radicals on collision. Moreover, the fact that fluorescence occurs in acetone at relatively high pressures is evidence of the comparative stability of the excited state. On the basis of a scheme consisting of reactions (1)—(8), together with reaction (9),

(9) $(CH_3)_2CO^* + CH_3{\cdot}CO \longrightarrow (CH_3)_2CO + CH_3 + CO$

and on the same assumption as before relative to the stationary concentrations of methyl and acetyl, the expression $d[C_2H_6]/d[CO] = (1 + k'\sqrt{I})/(k'' + k'''\sqrt{I} + k''''/\sqrt{I})$ can be derived. It has also been assumed that the quanta absorbed in the banded region and in the continuum are proportional to one another. This will be correct so long as the acetone pressure remains constant. Giving suitable numerical values to the constants, we obtain

$$C_2H_6/(CO) = (1 + 0{\cdot}001\sqrt{I})/(0{\cdot}35 + 0{\cdot}145\sqrt{I} + 0{\cdot}05/\sqrt{I}).$$

The curve plotted in Fig. 3 represents this relation. Although the early data from Table I, *a* lie somewhat below the line at high intensities, later experiments with a more refined technique (Table I, *b*) gave results in close agreement with the theory. Reaction (9), which represents the supposed interaction of the products of absorption in the banded region with those of the continuum, is therefore responsible for the decrease in the ratio at higher intensities.

The Influence of Temperature.—Careful repetition of Norrish, Crone, and Saltmarsh's experiments at 60° failed to confirm their claim that with pure acetone and with filtered light of low intensity, the sole products are carbon monoxide and ethane in equal volume. For similar rates of decomposition, we found 27·8% of methane in the gaseous products and a C_2H_6/CO ratio of 0·37. On the other hand, our analytical data for the full arc (Table IV) are in agreement with the results of their refluxing experiments (*loc. cit.*), which gave CO, 46·6; CH_4, 9·2; C_2H_6, 44·2%. Methane is therefore one of the major products of reaction under these conditions and its appearance is not due to the presence of liquid acetone, as Norrish has suggested. When a series of experiments with about 70 mm. of acetone at different temperatures are compared, the C_2H_6/CO ratio is found to approach unity with rise of temperature (Table V). Very little methane was formed at this pressure. The proportion of methane in the products at 60° increases therefore (*a*) with the acetone pressure and (*b*) when the light intensity is diminished (Table IV). This behaviour can be accounted for by a scheme first proposed to explain the thermal decomposition of acetone (Rice and Herzfeld, *J. Amer. Chem. Soc.*, 1934, **56**, 284; Rice, Rodowskas, and Lewis, *ibid.*, p. 2457) and applied later to the photo-decomposition at high temperatures (Leermakers, *loc. cit.*; Patat, *Z. physikal. Chem.*, 1935, *B*, **31**, 105), *viz.*,

(1) $(CH_3)_2CO + h\nu \longrightarrow CH_3 + CH_3{\cdot}CO$ (2) $2CH_3 \longrightarrow C_2H_6$
(4) $CH_3 + CH_3{\cdot}CO \longrightarrow C_2H_6 + CO$ (5) $CH_3{\cdot}CO \longrightarrow CH_3 + CO$
(10) $CH_3 + (CH_3)_2CO \longrightarrow CH_4 + {\cdot}CH_2{\cdot}CO{\cdot}CH_3$

The radical $\cdot CH_2{\cdot}CO{\cdot}CH_3$ combines either with itself to form acetonylacetone or with a methyl radical, giving methyl ethyl ketone. The only difference between this and the low-temperature scheme for the continuum lies in the inclusion of reaction (10). The reaction yielding diacetyl is omitted as this obviously is not formed. According to Leermakers, reaction (10) occurs readily at 400° but not at 200°, since the products not condensed by liquid air contain 33·3% of carbon monoxide at 400° and 50% at 200°. The remaining 66·6% at 400° was assumed to be methane, yet although gas analyses were not carried out, the remaining 50% at 200° was taken to be ethane. We have found, however, that ethane can be quantitatively removed by liquid air, and there seems to be little doubt that at 200° the residual gas was methane and not ethane as previously supposed. These results indicate therefore, that reaction (10) occurs readily at 200°, and our experiments show that it already begins to be of importance at 60°. With 80 mm. pressure of acetone, methyl groups disappear by other reactions, but as the pressure is increased to 840 mm., collisions with acetone become more frequent, until 20% of methane is produced by reaction (10). Furthermore, when the light intensity is decreased, methyl radicals suffer fewer collisions with one another and with acetyl, with the result that reaction (10) becomes of greater importance, in agreement with the observed increase in the percentage of methane.

Our previous conclusions with regard to the stability of the acetyl radical (*Nature*, 1936, **138**, 206) are fully confirmed by the results given in Table V. As the temperature is reduced, the ratio C_2H_6/CO and the amount of diacetyl formed steadily increase, and

the reaction tends to take the course $(CH_3)_2CO + h\nu \longrightarrow CH_3 + CH_3{\cdot}CO \longrightarrow 0{\cdot}5C_2H_6 + 0{\cdot}5(CH_3{\cdot}CO)_2$. The acetyl radicals are therefore comparatively stable at 0°, but at 60° all are decomposed by collisions in the gas phase (cf. high-pressure experiments, Table IV) or at the wall of the vessel (cf. p. 358 and Table V). Glazebrook and Pearson (private communication) have made a direct investigation of the acetyl radical by the mirror method and have arrived at similar conclusions.

There can now be no doubt that, from the chemical point of view, the photo-decomposition of acetone is not an essentially simple process accompanied by relatively unimportant side reactions, but that any one of several more or less complicated courses is possible under each set of conditions. It is proposed to extend the investigation by a detailed study of the quantum yield.

SUMMARY.

The absorption of light by acetone in the region of continuous absorption yields methane, ethane, carbon monoxide, and diacetyl, as a result of the primary process, $(CH_3)_2CO + h\nu \longrightarrow CH_3 + CH_3{\cdot}CO$.

The ratio C_2H_6/CO increases with increasing intensity of continuum light to a maximum value of about 2·5, and an equation has been deduced from a probable mechanism which accounts for this behaviour.

It is suggested that light absorption in the banded region leads to the production of an excited molecule which may dissociate directly into ethane and carbon monoxide without the intervention of radicals.

With the full light of the mercury arc at 20°, the ratio C_2H_6/CO increases to a maximum value of about 1·9, and then decreases to 1·5 as the light intensity is increased. This can be explained if it is supposed that the excited molecules produced in the band region interact with acetyl radicals arising from the absorption of light in the continuum.

The effective life of the acetyl radical rapidly decreases as the temperature is raised. Increase of acetone pressure or decrease of light intensity increases the proportion of methane in the products at 60°, owing to the operation of the reaction

$$CH_3 + (CH_3)_2CO \longrightarrow CH_4 + {\cdot}CH_2{\cdot}CO{\cdot}CH_3.$$

We thank the Chemical Society for a grant towards the cost of apparatus.

THE UNIVERSITY, LEEDS. [*Received, January 11th*, 1937.]

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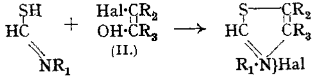
72. *Thioformylation of Amines.*

By A. R. TODD, F. BERGEL, KARIMULLAH, and R. KELLER.

IN the course of synthetic investigations in the aneurin series it was found that thiazolium salts of type (III), to which aneurin itself belongs, could be synthesised by condensation of thioformamido-compounds (I) with α-halogenated ketones (II) (Todd, Bergel, and Karimullah, *Ber.*, 1936, **69**, 217; J., 1936, 1557; Clarke and Gurin, *J. Amer. Chem. Soc.*, 1935, **57**, 1876).

(I.)  (II.) (III.)

Thioformamido-compounds have hitherto been prepared either by treatment of the corresponding formamido-compounds with phosphorus pentasulphide or by the addition of hydrogen sulphide to *iso*nitriles. The first of these methods is not capable of general application, and is in any case useless save with very stable compounds; the scope of the second is limited by the difficulty of obtaining appropriate *iso*nitriles.

The reaction between *iso*cyanates or *iso*thiocyanates and carboxylic acids, originally described by Wurtz (*Jahresber.*, 1851, 501; 1854, 566) and recently investigated by Nägeli

and Tyabji (*Helv. Chim. Acta*, **1934**, **17**, 947; 1935, **18**, 142), leads to formation of acylamides according to the scheme:

$$NR_1{:}C{:}O + R_2{\cdot}CO_2H \longrightarrow NHR_1{\cdot}CO{\cdot}O{\cdot}CO{\cdot}R_2 \xrightarrow{\text{heat}} NHR_1{\cdot}CO{\cdot}R_2 + CO_2$$

By replacing the carboxylic acid in the above reaction by a thiolthionic acid (R·CS·SH), thioacylamides can be obtained with elimination of carbonyl sulphide (or, if a thiocyanate is employed, carbon disulphide). By using dithioformic acid, thioformamido-compounds can be prepared in good yield, but here again the value of the method is governed by the accessibility of the *iso*cyanates.

Thioformylation of 5-aminopyrimidines can be effected by mixing aqueous solutions of the amine and potassium dithioformate or dithioformic acid at room temperature (Todd, Bergel, and Karimullah, J., 1936, 1557). The ease with which this reaction occurs led us to test its application to a variety of compounds containing amino- or imino-groups, partly to have available intermediates for thiazolium salt syntheses, and partly in the hope that the thioformyl derivatives might be of value in the separation and identification of amines generally. Thioformylation with potassium dithioformate has been found to be of general application, and methods are now described for carrying out the reaction with amines of widely varying types.

The aliphatic thioformamido-compounds prepared, except that from ethylenediamine, are liquids which, as such, are unsuitable for identification purposes, although they condense readily with amines to give substituted formamidines and with α-halogenated ketones to give thiazolium salts. Thioformylation of aromatic and heterocyclic amines yields crystalline derivatives, usually with sharp melting points, which are useful for identification. No thioformylation occurs with indole, diphenylamine, or methylaniline. From *o*-phenylenediamine an unstable thioformyl derivative can be obtained which passes slowly into benziminazole. With *o*-aminobenzylamine, potassium dithioformate even at room temperature causes immediate production of dihydroquinazoline; no thioformyl derivative could be obtained. The ease with which ring closure occurs in these cases suggests that thioacylamido-derivatives might advantageously be employed in such reactions where acylamido-derivatives are commonly used.

The interaction of dithioformic acid and ammonia may be used for the preparation of thioformamide, the yield being rather better than that obtained in the normal preparation from formamide and phosphorus pentasulphide (Willstätter and Wirth, *Ber.*, 1909, **42**, 1911).

Experimental.

Potassium Dithioformate.—The preparation from chloroform and potassium sulphide (Levi, *Atti R. Accad. Lincei*, 1923, **32**, I, 569) is satisfactory, the yield of recrystallised salt being about 45% of the theoretical.

Dithioformic Acid.—Prepared from the potassium salt according to Levi (*loc. cit.*), the acid is obtained as a cream-coloured, amorphous powder, the reactivity of which diminishes rapidly on keeping. Levi considered the free acid to be termolecular, but it is clear from molecular-weight determinations that it undergoes progressive polymerisation on keeping, which accounts for the diminishing activity (Found, by cryoscopic method in dioxan: after 2 hours, *M*, 154; after 24 hours, *M*, 555; after 72 hours, *M*, 666. Calc. for CH_2S_2: *M*, 78). Dithioformic acid is best kept in the form of its stable potassium salt, from which it can readily be prepared as required.

Action of Thiolthionic Acids on iso*Cyanates and* iso*Thiocyanates.*—(a) *Phenyl* iso*cyanate.* To a solution of phenyl *iso*cyanate (2 g.) in toluene (*ca.* 10 c.c.), dry, freshly precipitated dithioformic acid (2 g.) was added in portions. When the vigorous reaction had subsided, the semi-solid mass was left over-night, then heated on the water-bath until evolution of carbonyl sulphide ceased and practically everything was in solution (about 2 hours). On removal of the toluene and crystallisation of the residue from water, thioformanilide (2 g.), m. p. 138°, was obtained. When the dithioformic acid in the above preparation was replaced by dithioacetic acid, thioacetanilide, m. p. 75°, was obtained.

(b) *Phenyl* iso*thiocyanate.* A solution of phenyl *iso*thiocyanate (3 g.) in toluene (10 c.c.), treated with dithioformic acid (2 g.) in the manner above described, gave thioformanilide with

evolution of carbon disulphide. Yield, 2 g.; m. p. 138°. A similar experiment with dithioacetic acid gave thioacetanilide, m. p. 75°, in good yield.

General Methods for Thioformylation of Amines.—I. *For amines insoluble or sparingly soluble in water.* The amine, dissolved in ether or chloroform, is shaken with a slight excess of potassium dithioformate. On evaporation of the organic solvent the thioformyl product separates. Alternatively, the whole operation may be carried out in aqueous-alcoholic solution, and the product precipitated by addition of water.

II. *For amines soluble in water.* An aqueous solution of amine or one of its salts is mixed with excess of potassium dithioformate solution; the derivative separates on standing.

III. *For amines giving water-soluble thioformyl derivatives.* In this case, it is generally more convenient to shake together the amine and dithioformic acid in ether or dioxan solution till evolution of hydrogen sulphide ceases, and then remove the solvent by distillation. Alternatively, the amine hydrochloride and potassium dithioformate are shaken together in absolute alcohol.

Examples of Method I.—*Aniline.* The base (9·3 g.), dissolved in alcohol (20 c.c.), was added to a solution of potassium dithioformate (12 g.) in water (20 c.c.). Separation of thioformanilide soon began, and was complete in 2 hours. Water was added, and the crystalline product collected and recrystallised from hot water. Yield, quantitative.

By the same method, thioform-*o*-toluidide, m. p. 97°, was obtained from *o*-toluidine.

6-Aminoquinoline. To a solution of potassium dithioformate (1·5 g.) in water (25 c.c.) was added 6-aminoquinoline (1 g.) dissolved in chloroform, and the mixture was shaken for a few minutes. By bubbling nitrogen through the mixture, the chloroform was gradually evaporated, leaving the *thioformyl* derivative suspended in the aqueous solution; it crystallised from acetone–light petroleum in faintly yellow needles, m. p. 236° (Found: S, 16·6. $C_{10}H_8N_2S$ requires S, 17·0%); yield, quantitative.

Examples of Method II.—*5-Aminopyrimidines.* See Todd, Bergel, and Karimullah (*loc. cit.*).

Tryptamine. To tryptamine hydrochloride (500 mg.), dissolved in water (80 c.c.), was added potassium dithioformate (400 mg.). After 15 minutes the solution became turbid and an oil separated which slowly crystallised. Recrystallised from chloroform–light petroleum (b. p. 60—80°), the *product* formed large plates, m. p. 82° (Found: S, 15·1; N, 13·7. $C_{11}H_{12}N_2S$ requires S, 15·7; N, 13·7%).

Mezcaline. Mezcaline sulphate (200 mg.) and potassium dithioformate (150 mg.) in water (20 c.c.) deposited after 20 minutes an oil which slowly crystallised; it separated from acetone–light petroleum in colourless prisms, m. p. 92° (Found: N, 5·7; S, 12·2. $C_{12}H_{17}O_3NS$ requires N, 5·5; S, 12·5%). Yield, quantitative.

o-*Phenylenediamine.* An aqueous solution of the amine gave with potassium dithioformate at 0° an unstable thioformyl derivative, m. p. 77°, which even at room temperature changed rapidly into benziminazole, m. p. 170°. At temperatures above 0° the sole product was benziminazole.

*Monoacetyl-*o*-phenylenediamine.* The *thioformyl* derivative crystallised from acetone–light petroleum in colourless needles, m. p. 173° (Found: C, 55·7; H, 5·3; S, 16·3. $C_9H_{10}ON_2S$ requires C, 55·7; H, 5·1; S, 16·4%). Yield, quantitative.

Benzylamine and o-*nitrobenzylamine.* The *thioformyl* derivatives have m. p. 64° (Found: S, 20·7. C_8H_9NS requires S, 21·2%) and m. p. 94° (Found: S, 15·9. $C_8H_8O_2N_2S$ requires S, 16·3%), respectively.

o-*Aminobenzylamine.* The amine reacted readily with potassium dithioformate in aqueous solution even at room temperature, to give dihydroquinazoline, m. p. 128—129°, in quantitative yield.

Ethylenediamine. With potassium dithioformate *ethylenebisthioformamide*, m. p. 146—147°, is formed (Found: N, 18·8. $C_4H_8N_2S_2$ requires N, 18·9%).

Examples of Method III.—From dimethylamine, diethylamine, and piperidine or their hydrochlorides, thioformyl derivatives were obtained as yellow liquids with the properties recorded by Willstätter and Wirth (*Ber.*, 1909, **42**, 1920), and ethylamine gave the product described by Nef (*Annalen*, 1894, **280**, 297).

*N-iso*Amylthioformamide, prepared from *iso*amylamine and dithioformic acid in ethereal solution, had b. p. 143—146°/10 mm.; condensation with ω-bromoacetophenone and subsequent treatment with picric acid gave *4-phenyl-3-*iso*amylthiazolium picrate*, m. p. 101° (Found: N, 11·8. $C_{20}H_{20}O_7N_4S$ requires N, 12·1%).

Thioformamide. Aqueous ammonia (12 g.; *d* 0·880) is added with stirring to a suspension of dithioformic acid (7·8 g.) in ether (50 c.c.). After standing for 2 days at room temperature

the ethereal layer is separated, and the aqueous layer extracted several times with small quantities of ether. The combined ethereal solution and extracts are dried over phosphoric oxide, and the ether evaporated. The resulting syrup may be used directly as thioformamide for all ordinary purposes. To obtain solid thioformamide, the dried ethereal solution is concentrated to small bulk (20 c.c.), cooled to − 15°, and precipitated with light petroleum; yield, *ca.* 30%.

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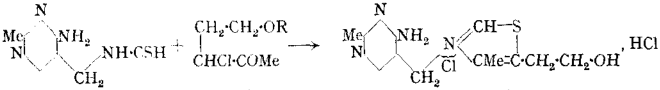
73. *Aneurin. Part VII. A Synthesis of Aneurin.*

By A. R. TODD and F. BERGEL.

WILLIAMS and CLINE (*J. Amer. Chem. Soc.*, 1936, **58**, 1504) have reported a synthesis of aneurin (III) and indicated briefly the route they employed. No details have yet been published, nor are details available of the synthesis carried out by the I. G. Farbenindustrie A. G. (cf. Grewe, *Z. physiol. Chem.*, 1936, **242**, 89). Both appear to be carried out by the addition of 4-amino-5-bromomethyl-2-methylpyrimidine to 5-β-hydroxyethyl-4-methylthiazole.

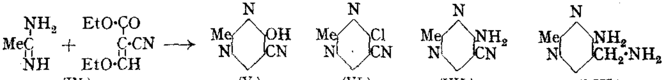
We have synthesised the vitamin by a method which is an extension of that already described for 3-pyrimidylthiazolium salts (Part V; J., 1936, 1559) and depends on the condensation of *4-amino-5-thioformamidomethyl-2-methylpyrimidine* (I) with methyl α-chloro-γ-hydroxypropyl ketone (II; R = H) or one of its derivatives.



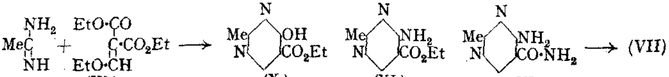
(I.) (II.) (III.)

For the synthesis of (I) we at first endeavoured to utilise as a starting material ethyl 4-hydroxy-2-methylpyrimidine-5-acetate (cf. Part VI; J., 1936, 1601), but all attempts to modify the Curtius or Hofmann degradation with this ester and its derivatives so as to produce the desired 4-amino-5-aminomethyl-2-methylpyrimidine failed, the low resistance of the amino-group in position 4 to hydrolytic agents invariably causing production of 4-hydroxy-5-aminomethyl-2-methylpyrimidine; the latter compound, too, could not be chlorinated. On the other hand, attempts to aminate 4-chloro-5-chloromethyl-2-methylpyrimidine led to formation of secondary amines; consequently the use of compounds of this series was abandoned.

Condensation of acetamidine with ethyl α-ethoxymethylene-α-cyanoacetate (IV) in absolute alcoholic solution gave an intermediate compound, probably ethyl α-cyano-β-acetamidinoacrylate, which on heating with alkali yielded *4-hydroxy-5-cyano-2-methylpyrimidine* (V). Refluxing with phosphoryl chloride afforded *4-chloro-5-cyano-2-methylpyrimidine* (VI), which could be aminated to give 4-amino-5-cyano-2-methylpyrimidine (VII); (VII) gave on catalytic hydrogenation 4-amino-5-aminomethyl-2-methylpyrimidine (VIII), isolated as its hydrochloride. The compound (VII) has been prepared in a different way by Grewe (*loc. cit.*), who also describes its reduction to the diamine.



(IV.) (V.) (VI.) (VII.) (VIII.)



(IX.) (X.) (XI.) (XII.)

An alternative route for the synthesis of (VII), which, though slightly longer, uses a cheaper starting material and is perhaps more reliable than the above, is the following. Ethyl ethoxymethylenemalonate (IX) condensed readily with acetamidine in presence of sodium ethoxide to give *ethyl 4-hydroxy-2-methylpyrimidine-5-carboxylate* (X), which, after successive chlorination with phosphoryl chloride and heating with alcoholic ammonia under pressure, yielded *ethyl 4-amino-2-methylpyrimidine-5-carboxylate* (XI). After conversion of (XI) into the corresponding *amide* (XII) with concentrated aqueous ammonia, the product was dehydrated to give the nitrile (VII), which could then be reduced as above mentioned. From (VIII), 4-amino-5-thioformamidomethyl-2-methylpyrimidine (I) was readily obtained by treatment with aqueous potassium dithioformate (cf. preceding paper).

The way now seemed clear for the synthesis of aneurin. As a result of our experience in the synthesis of 3-pyrimidylthiazolium salts (Part V, *loc. cit.*) we first endeavoured to condense (I) in the form of its sodium derivative with methyl α-chloro-γ-hydroxypropyl ketone (II; R = H) (Part III; J., 1936, 1555; Buchman, *J. Amer. Chem. Soc.*, 1936, **58**, 1803), but although various conditions were tried, only traces of aneurin could be obtained, the main product being the hydrochloride of (VIII). The reason for these failures may have lain in the instability of the sodium derivative. Compounds (I) and (II; R = H) did not yield aneurin when heated together in dioxan solution, but when a mixture of the two compounds alone was heated at 140° reaction occurred with considerable darkening and resinification. From the product a substance was isolated in poor yield which had the properties of aneurin. The low reactivity of the hydroxy-ketone (II; R = H), which probably exists mainly in the cyclic oxide form (cf. Buchman, *loc. cit.*), has already been mentioned (Part V, *loc. cit.*). Accordingly we heated a mixture of (I) and methyl α-chloro-γ-acetoxypropyl ketone (II; R = Ac) (Part III, *loc. cit.*) at 115—120° for a few minutes; smooth reaction occurred with production of a brownish-yellow mass, which crystallised on trituration with hot absolute alcohol containing a trace of hydrogen chloride. After recrystallisation from alcohol a product was obtained, m. p. 233—234°, having all the properties of aneurin chloride obtained from natural sources. The acetyl group in the ketone (II; R = Ac) is apparently eliminated in the reaction; this might be most readily explained by assuming that this compound also exists largely in the cyclic oxide form.

The synthetic material could not be distinguished from the natural vitamin by the formaldehyde-azo-test (Kinnersley and Peters, *Biochem. J.*, 1934, **28**, 667) or the thiochrome test (Part I; *Ber.*, 1935, **68**, 2257) and it showed a similar biological activity (380,000 I. U. per g.; natural vitamin, 400,000 I. U. per g.) as measured by the electrocardiagraphic method on rats (Birch and Harris, *Biochem. J.*, 1934, **28**, 602). Natural aneurin chloride isolated from rice polishings usually shows a m. p. 249—250° when pure, but a low-melting form has been reported by Kinnersley, O'Brien, and Peters (*Biochem. J.*, 1935, **29**, 701), who give m. p. 230° ± 2°; Williams and Cline (*loc. cit.*) state that their synthetic chloride has m. p. 232—234°. Our synthetic product apparently corresponds to the latter, but we do not consider the difference in m. p. is due to stereoisomerism as was tentatively suggested by Williams and Cline; it seems more probable that the existence of two forms of equal biological potency is due to dimorphism, a phenomenon which has been noticed by Kinnersley, O'Brien, and Peters (*loc. cit.*) in the case of the sulphate. Mixed with natural aneurin of m. p. 249°, the synthetic material had m. p. 243—246°. In accordance with this view we have compared the picrolonates prepared from the natural and the synthetic vitamin (see p. 367). Further, by oxidation of the synthetic vitamin with potassium ferricyanide in alkaline solution we have obtained a product, m. p. 225—226°, identical in every respect with thiochrome prepared either from natural aneurin or synthetically (Part VI, *loc. cit.*).

The synthesis of analogues of aneurin with a view to the determination of the necessary substituents for biological activity in 3-pyrimidinomethyl-thiazolium salts will form the subject of a later communication.

Experimental.

4-Hydroxy-5-cyano-2-methylpyrimidine (V).—To an ice-cold solution of sodium (10·2 g.) in absolute alcohol (300 c.c.) was added acetamidine hydrochloride (41·4 g.); the mixture was shaken for a few minutes and quickly filtered from precipitated sodium chloride. To the cooled

filtrate was added ethyl α-ethoxymethylene-α-cyanoacetate (75 g.) (de Bollemont, *Compt. rend.*, 1899, **128**, 1340; *Bull. Soc. chim.*, 1901, **25**, 20) in portions with shaking. As the ester went into solution a yellow colour developed and almost immediately a crystalline substance began to separate. After standing overnight at 0°, the precipitate was collected; *it crystallised from* ethyl acetate *in colourless needles* (37 g.), m. p. 108—110° (Found: C, 52·7; H, 6·3; N, 23·1. $C_8H_{11}O_2N_3$ requires C, 53·0; H, 6·1; N, 23·2%). This product may be ethyl α-cyano-β-acetamidinoacrylate.

The above intermediate product (36 g.) was heated on the water-bath for 5 minutes with a solution of sodium hydroxide (9 g.) in water (360 c.c.). The yellow solution was cooled, acidified with acetic acid, and concentrated in a vacuum to about half the original volume. On standing, *4-hydroxy-5-cyano-2-methylpyrimidine* separated; it crystallised from water in fine colourless needles or rods (9 g.), m. p. 233—235° (Found: C, 53·3; H, 4·0; N, 30·8. $C_6H_5ON_3$ requires C, 53·3; H, 3·7; N, 31·1%).

Efforts were made to cause direct production of the pyrimidine so as to avoid, if possible, the losses involved in the ring closure of the intermediate ester with sodium hydroxide; for this purpose condensations were made at various temperatures with various amounts of sodium ethoxide but without satisfactory results.

4-Chloro-5-cyano-2-methylpyrimidine (VI).—When 4-hydroxy-5-cyano-2-methylpyrimidine (5 g.) was heated under reflux with phosphoryl chloride (15 c.c.) during 30 minutes, most of it dissolved to give a dark brown solution. After removal of phosphoryl chloride in a vacuum, the mixture was poured into ice-water, neutralised with potassium carbonate, and extracted with ether. After drying of the extract over sodium sulphate and removal of solvent, the *chloro-compound* remained as a reddish-yellow resin, pure enough for amination purposes. Recrystallised from light petroleum, it formed long colourless rods, m. p. 63—64° (Found: Cl, 22·6. $C_6H_4N_3Cl$ requires Cl, 23·1%). Yield, 60—70%.

4-Amino-5-cyano-2-methylpyrimidine (VII).—The above chloro-compound (2 g.) was heated with absolute-alcoholic ammonia (6 c.c. saturated at 0°) in a sealed tube at 100° during 4 hours. After removal of the alcohol and ammonia in a vacuum, the residue was boiled with *ca.* 100 c.c. of chloroform, and the solution filtered from ammonium chloride and evaporated. On recrystallising from methyl alcohol, the product formed colourless needles, m. p. 249° with partial sublimation (Grewe, *loc. cit.*, gives m. p. 249°) (Found: C, 54·0; H, 4·8. Calc. for $C_6H_6N_4$: C, 53·7; H, 4·5%). Yield, 40%.

Ethyl 4-Hydroxy-2-methylpyrimidine-5-carboxylate (X).—To a solution of sodium (12·8 g.) in absolute alcohol (500 c.c.) at 0° were added acetamidine hydrochloride (26·3 g.) and ethyl ethoxymethylenemalonate (60 g.) (Claisen, *Ber.*, 1893, **26**, 2731). After standing for 1 hour at room temperature, the mixture was heated on a water-bath under reflux for a further hour. After removal of most of the alcohol in a vacuum, the residue was diluted with water, and unchanged ester removed by extraction with ether. The aqueous solution was acidified with acetic acid, and the *pyrimidine* extracted with ethyl acetate. The residue obtained on evaporating the dried ethyl acetate solution crystallised from acetone in long woolly needles, m. p. 191° (Found: C, 52·8; H, 5·9. $C_8H_{10}O_3N_2$ requires C, 52·7; H, 5·5%). Yield, 60%.

Ethyl 4-Amino-2-methylpyrimidine-5-carboxylate (XI).—A mixture of the above ester (96 g.) and phosphoryl chloride (250 c.c.) was heated under reflux for 30 minutes. The red solution so formed was evaporated in a vacuum to remove phosphoryl chloride, and the resinous residue treated with a little ice-water, made alkaline with potassium carbonate, and extracted with chloroform. The dried chloroform solution on evaporation left the chloro-ester as a reddish oil, which without further purification was heated in an autoclave at 100° during 3 hours with 10 times its volume of absolute-alcoholic ammonia (4*N*). After cooling, the alcohol and excess of ammonia were removed under reduced pressure, and the residue recrystallised several times from water. The *product* formed long colourless needles, m. p. 120° (Found: N, 23·2. $C_8H_{11}O_2N_3$ requires N, 23·2%). Yield, 65%.

4-Amino-2-methylpyrimidine-5-carboxyamide (XII).—The above finely powdered amino-ester (50 g.) was shaken at room temperature with aqueous ammonia (320 c.c., *d* 0·880) during 36 hours. The needle-shaped crystals of the initial material disappeared gradually, although no apparent dissolution was observed. The *amide* was collected and recrystallised from absolute alcohol, forming small prisms, m. p. 264—265° (Found: N, 36·7. $C_6H_8ON_4$ requires N, 36·8%). Yield, 65%. A further small quantity was obtained by concentrating the ammoniacal mother-liquor.

4-Amino-5-cyano-2-methylpyrimidine (VII).—The above amide (2 g.) was heated under reflux with phosphoryl chloride (15 c.c.) during 2—3 hours, and the mixture then poured on ice, made

alkaline with potassium carbonate, and extracted with chloroform. After drying over sodium sulphate, the chloroform was removed; the residue crystallised from methyl alcohol in needles, m. p. 249° with partial sublimation, not depressed by 4-amino-5-cyano-2-methylpyrimidine prepared as described above. Yield, 50%.

When large quantities of material were used in this preparation, the yield of product diminished considerably; this may be due to the insolubility of the amide in phosphoryl chloride, and phosphorus pentachloride may be preferable on the large scale.

4-Amino-5-aminomethyl-2-methylpyrimidine Hydrochloride.—The above amino-nitrile in acetic acid solution was subjected to catalytic hydrogenation in presence of palladised charcoal (cf. Grewe, *loc. cit.*). The product had m. p. 264—265°. The same result was achieved with a platinum oxide catalyst, though the reduction was slower.

4-Amino-5-thioformamidomethyl-2-methylpyrimidine (I).—An aqueous solution of the above hydrochloride was neutralised with potassium bicarbonate, and a slight excess (*ca.* 1·2 mols.) of potassium dithioformate added. After a short time the *thioformyl* derivative separated. It crystallised from alcohol in colourless platelets, m. p. 187° (decomp.) (Found: C, 46·1; H, 5·5. $C_7H_{10}N_4S$ requires C, 46·1; H, 5·5%).

Aneurin Chloride (III).—A mixture of 4-amino-5-thioformamidomethyl-2-methylpyrimidine (500 mg.) and methyl α-chloro-γ-acetoxypropyl ketone (600 mg.) (Part III, *loc. cit.*) was heated in a paraffin-bath at 115—120° during 15 minutes. The mixture became liquid and then brownish and viscous, a thiazole-like odour becoming noticeable. The mass was cooled and triturated repeatedly with dry ether; it then fell to a yellowish-brown powder. This was collected and heated with *ca.* 3 c.c. of absolute alcohol containing a little hydrogen chloride; after a few moments the product began to crystallise without having completely dissolved. After cooling, it was collected and separated from a small amount of sparingly soluble 4-amino-5-aminomethyl-2-methylpyrimidine hydrochloride by fractional crystallisation from absolute alcohol. The product had m. p. 233—234°, unchanged by recrystallisation (Found: C, 40·5; H, 6·0; N, 15·5; S, 8·5; Cl, 20·1. Calc. for $C_{12}H_{18}ON_4Cl_2S,H_2O$: C, 40·6; H, 5·6; N, 15·8; S, 9·0; Cl, 20·0%).

Comparison of Natural and Synthetic Aneurin Chloride.—In addition to the tests mentioned on p. 365, the following experiments were made. Treatment with cold aqueous picrolonic acid caused with each sample separation of yellow needles of a picrolonate, m. p. and mixed m. p. 164—165°; recrystallisation of this product from water in the ordinary way gave in each case a mixture of needles and prisms, m. p. 170—180°, not depressed on mixing. When this material was heated for 5 minutes with a small amount of water—insufficient to dissolve it completely—and the solution filtered hot, the residue consisted of prisms, m. p. 228—229° (decomp.). A mixed m. p. showed no depression. These results correspond exactly to the data for the dimorphous aneurin picrolonate described by Windaus, Tschesche, Laqueur, and Schultz (*Z. physiol. Chem.*, 1933, **204**, 123).

The only apparent difference in the two chlorides lay in the m. p., our specimen from natural sources having m. p. 249—250°, the synthetic material 233—234°, and a mixture of the two 243—246°. On seeding a solution of the synthetic product with a crystal of the natural, we obtained a product, m. p. 245—247°; a solution of the natural vitamin seeded with the synthetic gave crystals, m. p. 241—244°.* In all cases the crystals appeared to be colourless platelets. In view of these facts and the formation of the dimorphous picrolonate we are of the opinion that aneurin chloride is itself dimorphous.

We are indebted to the Beit Memorial Trustees for the support accorded to one of us (A. R. T.) in the earlier stages of this investigation; also to the Rockefeller Foundation for a grant to Prof. G. Barger, in whose laboratory the work was initiated, and for whose continued interest we express our thanks. We also thank Sir Gilbert Morgan of the Chemical Research Laboratory, Teddington, for the use of an autoclave.

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* (Note added, March 2nd). Since the above was written the interconversion of the two forms of the chloride has also been reported by Williams and Cline (*J. Amer. Chem. Soc.*, 1937, **59**, 216).

74. *The Stereoisomeric* 2 : 3 : 5 : 6-*Tetramethylpiperazines. Part V.*

By Frederic B. Kipping.

It has already been shown (J., 1929, 2889) that when 2 : 3 : 5 : 6-tetramethylpyrazine is reduced under various conditions, four of the five theoretically possible 2 : 3 : 5 : 6-tetramethylpiperazines are formed. Three of these bases, the α-, β-, and γ-isomerides, were obtained in quantity and further investigated (J., 1931, 1160; 1932, 1336; 1933, 143), but only very small amounts of the δ-compound were present in the reduction products and the fifth isomeride could not be isolated. 2 : 3 : 5 : 6-Tetramethylpiperazine is now prepared technically by the Shell Chemical Company by the reduction of tetramethylpyrazine with hydrogen under pressure and at a high temperature, either with or without a catalyst; it was anticipated that the investigation of large quantities of this material might lead to the isolation of the missing isomeride, and that possibly the δ-base might be obtained in amount sufficient for further study. About 1700 g. of this product were therefore submitted to examination; it was found to consist almost entirely (99—99·5%) of the α- and the β-base, but 1·2 g. of the δ-dihydrochloride and 3·7 g. of the *dinitroso*-derivative of a new base (ε) were isolated, together with a minute amount of unreduced tetramethylpyrazine. It is remarkable that the mixture apparently contains none of the γ-isomeride, which is the main product of the catalytic reduction at the ordinary temperature (J., 1929, 2892).

Experimental.

The 2 : 3 : 5 : 6-tetramethylpiperazine (1720 g.) was first separated, by draining at room temperature, into a solid (1390 g.; *A*), and a liquid fraction (329 g.; *B*). The solid portion at 40—45° furnished a liquid (65 g.; *C*), which solidified almost completely at room temperature, and a solid, m. p. 44—45° (1325 g.; *D*) (α-tetramethylpiperazine has m. p. 45°; *loc. cit.*, p. 2894). The liquid portion at 0° gave a liquid (197 g.; *E*) and a solid (132 g.; *F*). The liquid *E* was fractionally distilled and collected at 176—178°, 178—180°, and 180—182°. Each fraction gave a dinitroso-derivative, m. p. 130—140°, and all were therefore neutralised with hydrochloric acid, and the solutions evaporated: α-tetramethylpiperazine dihydrochloride separated in a pure state, and successive crops proved identical until a residue was obtained which did not crystallise easily and gave a dinitroso-derivative melting below 100°. This residue was converted entirely into dinitroso-derivative, which, after crystallisation from alcohol, yielded that of the β-base (m. p. 102°). A small residue undistilled in the original fractionation also gave some pure β-dinitroso-derivative.

Fractions *C*, *F*, and *D* (115 g. only) were treated in the same way and furnished further quantities of the α-dihydrochloride and the β-dinitroso-compound. In all, 511 g. of α-hydrochloride and 196 g. of the β-dinitroso-derivative were obtained. Evaporation of the mother-liquors of the dinitroso-derivatives gave fractions melting indefinitely from 83—85° up to 100°, and from mixed m. p. determinations all appeared to be similar. As it was thought that these consisted of mixtures of the α- and the β-compound, synthetic mixtures were prepared for comparison; it was found, however, that no mixture melted below 98—103·5° (this was given by a mixture of 10% α-, 90% β-), and therefore there must be some other base present. The whole of the residual dinitroso-derivative was accordingly hydrolysed and converted into a dihydriodide, which crystallised well: fractionation from water finally gave four fractions, each of which was reconverted into a dinitroso-derivative and further fractionated from alcohol and acetone. From the most soluble fraction of the dihydriodide, a little dinitroso-δ-tetramethylpiperazine was isolated, and from the least soluble a little of the corresponding α-derivative: the remainder of the fractions was separately hydrolysed and converted into the dibenzoates. That obtained from the least soluble dihydriodide furnished two fractions: (*a*) sparingly soluble in water, m. p. 236—238° (dinitroso-derivative, m. p. 157°), the α-base; (*b*) a more soluble fraction which, after crystallising from alcohol, had m. p. 163—165° and gave a dinitroso-derivative which, crystallised from alcohol and acetone, finally had m. p. 116°, the new ε-base. The remaining benzoates, after fractionation, conversion into dinitroso-derivatives, and fractionation, yielded mainly the β-base, together with a little more δ- and ε-.

The whole of the mother-liquors of dinitroso-derivatives which could not be further separated, was hydrolysed (14 g. of hydrochloride obtained) and reconverted into benzoates: the mixture was apparently so complex that separation proved impossible, and as all the tetramethyl

piperazines had now been obtained and the mixture could not therefore contain any new compound, experiments were abandoned

ε-2 : 3 : 5 : 6-*Tetramethylpiperazine dihydrochloride*, prepared from the dinitroso-derivative, crystallised from aqueous alcohol in small prisms (Found : Cl, 33·0. $C_8H_{18}N_2$,2HCl requires Cl, 33·0%). With alkali a solid base (or hydrate) was precipitated, m. p. 60°.

Dinitroso-ε-2 : 3 : 5 : 6-*tetramethylpiperazine* crystallised from alcohol or acetone in yellow prisms, m. p. 116—117° (Found : C, 48·1; H, 8·2; N, 27·9. $C_8H_{16}O_2N_4$ requires C, 48·0; H, 8·0; N, 28·0%). This m. p. was depressed by the addition of the α- or the β-derivative.

Dibenzoyl-ε-2 : 3 : 5 : 6-*tetramethylpiperazine* was easily prepared by the Schotten–Baumann method, and crystallised in needles from acetone (easily soluble) or light petroleum (sparingly soluble), m. p. 146—147° (Found : N, 8·0. $C_{22}H_{26}O_2N_2$ requires N, 8·0%).

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75. *Interaction of Arylated Unsaturated Substances with Diazonium Salts.*

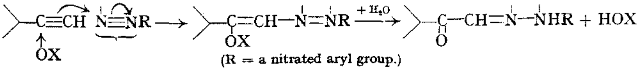
By A. D. AINLEY and ROBERT ROBINSON.

SCHARVIN and PLACHUTA (*J. Russ. Phys. Chem. Soc.*, 1916, **48**, 253) found that cuprous acetylide and benzenediazonium sulphate reacted with formation of diphenyl, tetraphenylethane, and other products. Henrich and Thomas (*Ber.*, 1907, **40**, 4924) obtained formazylacrylic acid from glutaconic acid and benzenediazonium chloride, and ethyl glutaconate gave a bisbenzeneazo-derivative, one of the azo-groups passing into the hydrazone tautomeric form. Meyer (*Ber.*, 1919, **52**, 1468) obtained nitro- and dinitro-benzeneazo-derivatives of the simpler, conjugated, doubly unsaturated hydrocarbons. Quilico and Freri (*Gazzetta*, 1928, **58**, 380) showed that anethole, *iso*safrole, and *iso*apiole are converted by nitro- or dinitro-benzenediazonium salts into the substituted phenylhydrazones of anisaldehyde, piperonal, and apiolealdehyde respectively (cf. Quilico and Fleischner, *ibid.*, 1929, **59**, 39; Quilico and Freri, *ibid.*, p. 600; *idem, ibid.*, 1930, **60**, 606). Another type of reaction, namely, displacement of the unsaturated side chain, was noted in the case of *p*-dimethylamino*iso*propenylbenzene, which, with *p*-nitrobenzenediazonium sulphate, was converted into *p*-nitrobenzeneazodimethylaniline (Quilico and Freri, *ibid.*, 1932, **62**, 253); the normal formation of dimethylaminobenzaldehyde-*p*-nitrophenylhydrazone had been previously observed under other conditions.

We have found that *p*-methoxystyrene undergoes Quilico's reaction with 2 : 4-dinitrobenzenediazonium sulphate in alcoholic solution and is converted into anisaldehyde-2 : 4-dinitrophenylhydrazone. This was to be anticipated in view of the close analogy with anethole; styrene, however, did not behave in a similar fashion and gave a very small yield of an unidentified substance.

p-Methoxyphenylacetylene was changed by *p*-nitrobenzenediazonium sulphate into a substance, $C_{15}H_{13}O_4N_3$, which is the p-*nitrophenylhydrazone* of p-*methoxyphenylglyoxal*, $MeO{\cdot}C_6H_4{\cdot}CO{\cdot}CH{:}N{\cdot}NH{\cdot}C_6H_4{\cdot}NO_2$. A similar substance was obtained when 2 : 4-dinitrobenzenediazonium sulphate was employed. Phenylacetylene gave *phenylglyoxal*-p-*nitrophenylhydrazone* in a like manner, but with 2 : 4-dinitrobenzenediazonium sulphate the product was of uncertain composition.

The mechanism of the process can be simply represented as follows :



(R = a nitrated aryl group.)

EXPERIMENTAL.

Anisaldehyde-2 : 4-dinitrophenylhydrazone.—A mixture of 2 : 4-dinitroaniline (3 g.), acetic acid (20 c.c.), and concentrated sulphuric acid (2 c.c.) was cooled in ice, and *iso*amyl nitrite (3 c.c.) introduced. The diazo-sulphate was precipitated by the addition of ether, collected, dissolved in alcohol (20 c.c.), and mixed with *p*-methoxystyrene (2·5 c.c.). A vigorous evolution of nitro-

gen occurred and after the solution had been kept for 24 hours at 0°, water was added and the precipitated oil was collected, washed, and dissolved in a little alcohol. The brick-red residual solid (1 g.) separated from acetic acid in bronze-red plates of anisaldehyde-2 : 4-dinitrophenylhydrazone, m. p. 249—250° (Found : C, 52·8; H, 3·8; N, 17·5. Calc. for $C_{14}H_{12}O_5N_4$: C, 53·1; H, 3·8; N, 17·7%), not depressed by an authentic specimen, m. p. 250—251°. No definite compound could be isolated from the mother-liquors.

In a similar experiment with styrene there was much less evidence of immediate reaction (such as darkening, gas evolution), but after 2 days at 0° small clusters of buff crystals, m. p. 76° (decomp.), had separated. The substance decomposed in alcohol, was readily soluble in water to a yellow solution, and gave a bluish-purple azo-compound with alkaline β-naphthol.

p-*Methoxyphenylglyoxal*-p-*nitrophenylhydrazone*.—A mixture of *p*-nitroaniline (5 g.), acetic acid (30 c.c.), and concentrated hydrochloric acid (5 c.c.) was cooled to 0°, and *iso*amyl nitrite (5 c.c.) gradually added. The oil precipitated by ether was washed with more ether, then mixed with alcohol (20 c.c.) and a solution of *p*-methoxyphenylacetylene (4 g.) in alcohol (20 c.c.). Separation of a brownish-yellow solid commenced almost at once and after 24 hours (some deterioration) it was collected (2·5 g.). It was extremely sparingly soluble in alcohol, very sparingly soluble in acetic acid, and moderately readily soluble in nitrobenzene. After several crystallisations from acetic acid, the *substance* was obtained in small, golden-yellow, rectangular plates, m. p. 261° (Found : C, 60·1; H, 3·9; N, 13·8. $C_{15}H_{13}O_4N_3$ requires C, 60·2; H, 4·3; N, 14·0%). It was insoluble in aqueous sodium hydroxide, but dissolved in the presence of acetone to a deep reddish-violet solution, the colour of which faded during 2—3 minutes to pale yellow. Water added to the orange-red solution in concentrated sulphuric acid precipitated the unchanged substance.

The analogous experiment with phenylacetylene (2·5 g.) gave a pale yellow solid (0·7 g.), which crystallised from acetic acid in long, thin, brownish-yellow plates, m. p. 252° (Found : C, 61·5, 61·3; H, 3·9, 3·8; N, 14·3. $C_{14}H_{11}O_3N_3,\frac{1}{4}C_2H_4O_2$ requires C, 61·3; H, 4·2; N, 14·8%). This substance is probably *phenylglyoxal*-p-*nitrophenylhydrazone*; its solubility relations and its behaviour with acetone and aqueous alkali and with sulphuric acid (crimson coloration) resemble those of the methoxy-derivative of more precise composition.

p-*Methoxyphenylglyoxal-2* : *4-dinitrophenylhydrazone*.—2 : 4-Dinitrobenzenediazonium sulphate (3 g. of the base) was prepared as above and mixed with alcohol (20 c.c.) and *p*-methoxyphenylacetylene (2 g.) at 0°. The solution quickly became dark reddish-brown and crystallisation began after 15 minutes. After 24 hours at 0° the solid was collected (3·1 g.) and crystallised from acetic acid, forming canary-yellow needles, m. p. 235° (Found : C, 52·2; H, 3·4; N, 16·2. $C_{15}H_{12}O_6N_4$ requires C, 52·3; H, 3·5; N, 16·3%). The *substance* is very sparingly soluble in alcohol or cold acetic acid and moderately readily soluble in hot acetic acid or cold nitrobenzene. It is insoluble in hot aqueous sodium hydroxide, but dissolves in the presence of alcohol or acetone to a deep cherry-red solution. On oxidation with potassium permanganate it afforded anisic acid, m. p. 181—182°.

The corresponding experiment with phenylacetylene (2 g.) gave less visible sign of reaction, but after 3½ days, rosettes of dark brown-red prisms with a greenish lustre had separated (0·7 g.). This substance exploded violently at 115° and for this reason the analytical results were inconsistent (Found : C, 45·3, 44·6; H, 3·0, 3·6; N, 23·3, 23·5%). It was certainly not a simple phenylhydrazone, because it decomposed with gas-evolution and tar-formation when treated with sodium hydroxide, and in the presence of sodium acetate it coupled with β-naphthol to a red azo-compound.

p-*Methoxyphenylglyoxalbis-2* : *4-dinitrophenyhydrazone*.—(A) The preparation of *p*-methoxyphenylglyoxal by an adaptation of the method of Riley, Morley, and Friend (J., 1934, 1875) gave very poor results in the absence of a solvent as recommended for the oxidation of acetophenone by selenium dioxide. In the presence of alcohol a small yield was obtained, but the keto-aldehyde was not completely separated from *p*-acetylanisole. A small fraction of nearly pure material was used and, by condensation with 2 : 4-dinitrophenylhydrazine (a little less than 1 mol.) in cold acetic acid solution containing a trace of hydrogen chloride, *p*-methoxyphenylglyoxal-2 : 4-dinitrophenylhydrazone was obtained. This specimen was crystallised from acetic acid; m. p. 234° alone or mixed with that obtained as described above (Found : C, 52·2; H, 3·4; N, 16·0%).

On condensation of *p*-methoxyphenylglyoxal with an excess of 2 : 4-dinitrophenylhydrazine in boiling acetic acid solution, a deep red, crystalline solid separated. This was almost insoluble in acetic acid, but crystallised from nitrobenzene in dark crimson needles, m. p. 292° alone or mixed with the specimen obtained as described in (B).

(B) The substance (0·3 g.), m. p. 235°, derived from *p*-methoxyphenylacetylene and 2 : 4-dinitrobenzenediazonium sulphate was refluxed for 1 hour with 2 : 4-dinitrophenylhydrazine (0·2 g.), concentrated hydrochloric acid (1 c.c.), and acetic acid (24 c.c.). The separated crystals (0·3 g.) were recrystallised from nitrobenzene; m. p. 292° (Found : C, 48·2; H, 3·2; N, 20·7. $C_{21}H_{16}O_9N_8$ requires C, 48·1; H, 3·1; N, 21·3%).

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Dyson Perrins Laboratory, Oxford University. [*Received, January 14th*, 1937.]

76. *The Oxidation of* cyclo*Hexanone and Suberone by Means of Caro's Acid.*

By Robert Robinson and Leonard Hart Smith.

The convenient preparation of 6-hydroxyhexoic and 7-hydroxyheptoic acids or their simple derivatives has become an object of investigation in connection with two different synthetical investigations in this laboratory. Many-stage syntheses have been proposed, and even recently used, in the case of 6-hydroxyhexoic acid, but these are obviously unsatisfactory in connection with such a simple substance. The most promising line of attack is the development of the method of Baeyer and Villiger (*Ber.*, 1899, **32**, 3625; 1900, **33**, 858) whereby ketopolymethylenes are oxidised by Caro's acid or an equivalent reagent. From suberone, for example, Baeyer and Villiger obtained, in the presence of alcohol, ethyl 7-hydroxyheptoate in a yield of 40%. Careful repetition of this work has made it clear that the reaction is more complex than would appear from the description. Under the specified conditions, carefully observed, the product was a mobile oil having an agreeable odour of pineapples, but this could not be distilled even in a high vacuum. The resulting very viscous material, after hydrolysis with alkali and treatment with hydriodic acid, afforded 7-iodoheptoic acid (the position of the iodine should perhaps be regarded as uncertain). Hence it seemed that the complex substances obtained on attempted distillation of the primary product were poly-esters. Accordingly, we modified the process as described by Baeyer and Villiger by adding a stage of re-esterification of the crude product by means of boiling alcoholic sulphuric acid. Ethyl 7-hydroxyheptoate could then be isolated, but even so the yield was sensitive to the conditions of the oxidation and especially to the temperature. At 0° some suberone peroxide was formed and some unchanged ketone was recovered; the best temperature was near 15°. It is not improbable that some manipulation equivalent to our re-esterification was actually employed by Baeyer and Villiger and thought to have little significance.

The oxidation of *cyclo*hexanone by the Baeyer–Villiger general method was first examined by Linstead and Rydon (J., 1934, 1999), who stated that the product was a high-boiling oil which could not be distilled without decomposition. This observation has been confirmed, but treatment of the crude product with boiling alcoholic sulphuric acid affords ethyl 6-hydroxyhexoate in useful yield, and for the first time the ω-substituted hexoic acids become readily accessible substances. Similarly, hexamethylene glycol becomes more available by applying the Bouveault–Blanc reduction method to the hydroxy-ester. We were unable to discover a satisfactory method for the oxidation of 4-methyl*cyclo*hexanone by Caro's acid.

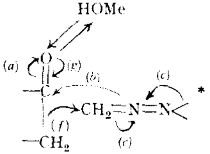
The oxidation of *cyclo*pentanone proceeds with eventual formation of *ethyl 5-hydroxyvalerate* in only moderate yield. The ester is mixed with an unsaturated by-product; there is a little of such a substance in the ethyl 6-hydroxyhexoate obtained as here described, but the specimen of ethyl 7-hydroxyheptoate was saturated.

The elegant method of Mosettig and Burger (*J. Amer. Chem. Soc.*, 1930, **52**, 3456) superseded all earlier processes for the preparation of suberone. We have found it convenient to adopt a few modifications in detail, and have isolated 1-hydroxymethyl*cyclo*hexan-1-ol as a by-product of the action of diazomethane on *cyclo*hexanone in the presence

of methyl alcohol and subsequent to the treatment of the products with aqueous sodium bisulphite. It seems probable that this glycol arises from the hydration of the corresponding ethylene oxide derivative obtained by Mosettig and Burger as a by-product (*loc. cit.*).

For the mechanism of this and similar ring enlargements, Mosettig and Burger approve the hypothesis of Meerwein and of Arndt involving the migration of radicals or their equivalent in the form of full free valencies. It seems, however, that the course of the process can be illustrated without making such an assumption if we combine the suggestions of Bradley and Robinson (J., 1928, **1312**) with the idea of electromeric vibrations of small, possibly very small, amplitude (Robinson, *Chem. News*, 1926, **133**, 7). The reaction occurs only in the presence of methyl alcohol, here regarded simply as a source of active proton, free or combined, which by reversible co-ordination with the oxygen of the carbonyl group through the unshared electrons of the oxygen atom initiates the process by inducing the electromeric change (*a*). This excitation of the carbonyl group by the catalyst results in an electron defect on the carbon atom, which is remedied by the attack of unshared electrons of the diazomethane (*b*).

The displacement (*b*) and its corollary (*c*) doubtless occur to some extent in the normal molecules, but go further when the strain on the carbon atom of the diazomethane is relieved in the course of reaction. Both are steps in the formation of the nitrogen molecule, which now asserts its autonomous character by taking charge of the electrons necessary for its independent existence (*c*). This produces, however, a defect of electrons on the diazomethane carbon, which must in consequence acquire other electrons from the oxygen atom (ethylene oxide formation, not represented) or from the nearest bond in the *cyclo*hexane ring (*f*). The latter change is synchronous with, or closely followed by, the reversal of (*a*), namely, (*g*). Alternations of (*a*) and (*g*) together with the unidirectional displacements (*b*)—(*f*) bring about the completion of the reaction in a continuous manner.



EXPERIMENTAL.

Suberone.—The method was essentially that of Mosettig and Burger (*loc. cit.*) with some improvements in the manipulation such as the use of more efficient fractionating columns and slight variations in the method of working up the product. *cyclo*Hexanone (73·2 g.) gave suberone (46·0 g., b. p. 67—68°/12 mm.), and the material that did not react with sodium bisulphite was fractionated as follows at 13—14 mm.: (1) 1·3 g., b. p. 40—74°; (2) 1·0 g., b. p. to 93°; (3) 0·8 g., b. p. to 100°; (4) 4·0 g., b. p. to 115°; (5) 1·8 g., b. p. 118—123°; (6) 6·0 g., b. p. to 132°; (7) 2·5 g., b. p. to 140°; (8) 2·8 g., b. p. 150—155°.

All fractions except (5) and (6) were liquid, and (1), (2), and (3) were ketonic (ready formation of dinitrophenylhydrazones); (2) was largely *cyclo*octanone, identified by the preparation of the semicarbazone and 2 : 4-dinitrophenylhydrazone (compare Mosettig and Burger). Fractions (5) and (6) solidified, and (6) was crystallised from benzene–light petroleum, forming colourless needles, m. p. 73·5—74° (Found: C, 64·8; H, 10·8. Calc. for $C_7H_{14}O_2$: C, 64·6; H, 10·7%). The substance is readily soluble in water, and in organic solvents with the exception of light petroleum. When heated in dilute sulphuric acid solution with potassium permanganate, *cyclo*hexanone was formed, and identified by analysis and by the preparation of the semicarbazone, m. p. 161—162° and m. p. 162—163° when mixed with an authentic specimen, m. p. 164—164·5°. The semicarbazone of suberone has m. p. 163—164°, but a mixture with *cyclo*hexanone semicarbazone shows a depression of 20°. This by-product is evidently 1-hydroxymethyl*cyclo*hexan-1-ol, which has m. p. 76—77° (Wallach and Isaac, *Annalen*, 1906, **347**, 331).

* This symbol was employed in 1928 in order to formulate the reactions of diazomethane on an electronic basis. It implies precisely the same view of the actual constitution of the substance as that based on the hypothesis of resonance, although it is certainly true that the latter theory suggests new ways of testing the validity of this and similar structures. The basic structural conceptions of the resonance theory in organic chemistry are not novel; what is new is the possibility of more searching analysis and the theoretical derivation and justification of the existing hypothesis of intermediate valency states.—R. R.

Ethyl 7-Hydroxyheptoate.—Potassium persulphate (50 g.) was gradually added to a well-stirred mixture of sulphuric acid (71 c.c., *d* 1·84) and water (24 c.c.) maintained below 15°; alcohol (100 c.c.) was then introduced, also below 15°. The temperature being kept *at* 15°, a mixture of suberone (10 g.) and alcohol (30 c.c.) was added during 1 hour, and stirring was continued for a further 1½ hours. The mixture was diluted to 1 litre, filtered, saturated with ammonium sulphate, and thoroughly extracted with ether. After removal of the solvent from the dried extract, the residue was mixed with alcohol (15 c.c.) and sulphuric acid (1 c.c.) and heated (bath at 110°) for 6 hours. The product was isolated by means of ether and distilled, b. p. 140—146°/12 mm. (nearly all at 142°) (7·5 g.), with a clear brown oily residue, b. p. 193°/0·5 mm. (Found: C, 64·3; H, 10·4. $C_{16}H_{30}O_5$ requires C, 63·6; H, 9·9%). This *substance* appears to be a di-ester of the formula $OH\cdot[CH_2]_6\cdot CO\cdot O\cdot[CH_2]_6\cdot CO_2Et$, since it furnished the hydrazide described below.

The main fraction, ethyl 7-hydroxyheptoate, afforded a *phenylurethane*, glistening white plates from light petroleum, m. p. 64—65° (Found: N, 4·9. $C_{16}H_{23}O_4N$ requires N, 4·8%), and a *hydrazide*, which crystallised from ethyl acetate as silky white needles, m. p. 121—123° (Found: N, 17·6. $C_7H_{16}O_2N_2$ requires N, 17·5%). In some experiments, under other conditions, the odour of pineapples was very pronounced, and in such cases the yield was diminished. The substance responsible for the odour is a volatile solid which we have not examined because our object was to avoid its formation. Taking into consideration the work of Natta, Hill, and Carothers (*J. Amer. Chem. Soc.*, 1934, **56**, 455) on the 14-membered ring dilactone related to 6-hydroxyhexoic acid, and of Ruzicka and Stoll (*Helv. Chim. Acta*, 1928, **11**, 1159) on the relation between odour and number of ring-members in large-ring lactones, it seems certain that this volatile odoriferous solid is the 16-membered ring dilactone related to 7-hydroxyheptoic acid.

Ethyl 6-Hydroxyhexoate.—The oxidising mixture was prepared as described above but with double quantities, and it was adjusted to 10°. *cyclo*Hexanone (19 g.) in alcohol (30 c.c.) was then added during 1 hour, and after a further 15 minutes the cooling bath was removed and stirring continued for 1 hour; the temperature finally reached was 15°. The product was isolated as in the previous case, then mixed with alcohol (50 c.c.) and sulphuric acid (4 c.c.) and refluxed for 6 hours. The esters were isolated as before, and on distillation, ethyl 6-hydroxyhexoate (14·7 g.), b. p. 134°/15 mm. (Found: C, 60·2; H, 9·9. Calc. for $C_8H_{16}O_3$: C, 60·0; H, 10·0%), was obtained; the residue was a pale yellow oil (3 g.), b. p. 158—160°/0·05 mm. or 191°/1·5 mm. (Found: C, 61·3; H, 9·4. $C_{14}H_{26}O_5$ requires C, 61·3; H, 9·5%), evidently consisting of *5-carbethoxyamyl 6-hydroxyhexoate*, $OH\cdot[CH_2]_5\cdot CO\cdot O\cdot[CH_2]_5\cdot CO_2Et$.

Ethyl 6-hydroxyhexoate forms a *phenylurethane*, white plates, m. p. 50—51° (Found: N, 5·1. $C_{15}H_{21}O_4N$ requires N, 5·0%), from light petroleum. In agreement with Natta, Hill, and Carothers (*loc. cit.*), the hydrazide had m. p. 115° and was also obtained from the above di-ester.

The method works well on a large scale; *cyclo*hexanone (95 g.) oxidised at 10° gave ethyl hydroxyhexoate (60 g.).

Small quantities of cyclo*hexanone peroxide* were formed in some of our experiments and constituted the solid precipitated when the oxidation mixture was diluted; the specimens, combined and crystallised from benzene, gave prisms, m. p. 128° (Found: C, 63·4; H, 8·8. $C_6H_{10}O_2$ requires C, 63·2; H, 8·8%). The substance had the usual character of ketone-peroxides; it was stable towards acid solutions of potassium iodide, but a red coloration gradually appeared when a solution in light petroleum was shaken with aqueous ferrous sulphate and ammonium thiocyanate.

Hexamethylene Glycol.—A mixture of ethyl hydroxyhexoate (12·5 g.) and anhydrous alcohol (50 c.c.) was rapidly added to sodium (10·8 g.) (bath at 140°) with the usual arrangements. After the initial reaction, more alcohol and then water were introduced, and the mixture was eventually acidified with hydrochloric acid, saturated with ammonium sulphate, and extracted with ethyl acetate. The product (6·0 g.) had b. p. 145—146°/16 mm., and solidified at once on cooling (cf. Bouveault and Blanc, *Bull. Soc. chim.*, 1904, **31**, 1204). A procedure analogous to that recommended in "Organic Syntheses" (**1**, 8) for the preparation of trimethylene bromide being adopted, the glycol (5·8 g.) gave hexamethylene dibromide (8·7 g., b. p. 110°/12 mm.) (steam-distillation of the dibromide would probably be an improvement).

Ethyl 5-Hydroxyvalerate.—The oxidation of *cyclo*pentanone (10 c.c.) was effected as described above but at −5° to 2°. After all the stages detailed above had been followed, *ethyl 5-hydroxyvalerate* (4·5 g.), b. p. 114°/14 mm., was isolated (Found: C, 58·5; H, 9·3. $C_7H_{14}O_3$ requires C, 57·5; H, 9·6%). The *hydrazide*, crystallised from ethyl acetate, had m. p. 105—106° (Found:

N, 20·9. $C_5H_{12}O_2N_2$ requires N, 21·2%). The high value for carbon in the case of the ester was found to be due to the presence of an unsaturated impurity.

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77. *The Action of Alkaline Reagents on Some Nitroso-α-arylamino-ketones and their Oximes.*

By J. CAMPBELL EARL and STANLEY J. HAZLEWOOD.

THE "nitrolamines" formed by the interaction of nitrosochlorides, nitrosites or nitrosates of ethylenic compounds with primary amines are themselves secondary amines and as such yield nitrosoamines when treated with nitrous acid (Wallach, *Annalen*, 1887, **241**, 290). Working with nitro-anilides and -toluidides derived from trimethylethylene nitrosate,

$$\begin{matrix} R_2C\cdot O\cdot NO \\ R'\cdot CH\cdot NO \end{matrix} \rightleftharpoons \begin{matrix} R_2C\cdot O\cdot NO \\ R'\cdot C{:}NOH \end{matrix} \xrightarrow{NH_2R''} \begin{matrix} R_2C\cdot NHR'' \\ R'\cdot C{:}NOH \end{matrix} \longrightarrow \begin{matrix} R_2C\cdot NR''\cdot NO \\ R'\cdot C{:}NOH \end{matrix}$$

Wallach noted that the nitroso-derivatives dissolved in sodium hydroxide solution and that, when the alkaline solutions were boiled, nitrogen was evolved and red tarry products formed. This reaction has now been further examined for derivatives not only of trimethylethylene but also of methyl-Δ^1-*cyclo*hexene, α-terpineol, and α-pinene. All such nitroso-α-anilino-ketoximes, when treated with an alkaline solution of β-naphthol, give rise to benzeneazo-β-naphthol, slowly in the cold and more quickly on warming, especially in aqueous-alcoholic solution.

By hydrolysing the nitrolamines with dilute mineral acid, the corresponding α-anilino-ketones are produced (Wallach, *loc. cit.*). These α-anilino-ketones readily yield nitroso-amines, which do not, however, react with alkaline β-naphthol solution. This behaviour is in contrast with that of certain nitroso-β-anilino-ketones (Jones and Kenner, J., 1933, 363), which, when subjected to the action of alkali in the presence of β-naphthol, give benzeneazo-β-naphthol. It appears from these results that the tendency of phenyl-nitrosoamines, $R\cdot N(NO)\cdot C_6H_5$, to fission by the action of alkali is strongly influenced by the nature of the group R. The presence of a keto-group in the appropriate position in the group R inhibits the tendency to breakdown, but the inhibition is overcome by oximation of the keto-group.

From trimethylethylenenitrosonitrolanilide, a secondary product of fission has been obtained. This is a well-crystallised, relatively stable substance, has the molecular composition $C_{16}H_{24}O_3N_4$, contains a nitroso-group, and is produced apparently by the condensation of one molecule of the nitrosonitrolanilide with one molecule of its hypothetical primary fission product, $OH\cdot CMe_2\cdot CMe{:}NOH$:

$$C_{11}H_{15}O_2N_3 + C_5H_{11}O_2N \longrightarrow C_{16}H_{24}O_3N_4 + H_2O.$$

Further examination of this product and its homologues, obtained by substituting *o*- and *p*-toluidine for aniline, together with an investigation of other structural types giving rise to similarly decomposable nitrosoamines, is in progress.

EXPERIMENTAL.

Preparation of α-Anilino-ketoximes.—The preparation of trimethylethylenenitrolanilide is typical. The method of Earl and Kenner (J., 1927, 1269) was first used, but a method similar to that employed by the same workers for the preparation of pinenenitrolanilide is simpler and equally satisfactory as regards yield.

A solution of trimethylethylenenitrosochloride (10 g.), aniline (8 g.), and crystallised sodium acetate (20 g.) in methylated spirit (100 ml.) was refluxed on a water-bath for 10 minutes and poured into an excess of ice-water. The product, after solidifying, was dissolved in glacial acetic acid, and the diluted solution filtered into concentrated aqueous ammonia cooled in ice; trimethylethylenenitrolanilide (13·5 g.) was obtained, m. p. 143° after recrystallisation from aqueous alcohol.

The following were similarly prepared: trimethylethylenenitrol-*p*-toluidide, m. p. 115°; trimethylethylenenitrol-*o*-toluidide, m. p. 109°; *methyl*-Δ^1-cyclo*hexenenitrolanilide*, m. p. 139° (Found: N, 12·85. $C_{13}H_{18}ON_2$ requires N, 12·9%); and α-terpineolnitrolanilide, m. p. 149°.

Preparation of Nitroso-α-anilino-ketoximes.—The case of trimethylethylene is again typical. A solution of the nitrolanilide of trimethylethylene (6 g.) in excess of dilute hydrochloric acid was cooled with ice and slowly treated with aqueous sodium nitrite until no further precipitate was formed. The pale yellow, flocculent nitrosoamine (6 g.) was filtered off almost immediately; after solution in chloroform and precipitation with light petroleum (b. p. 60—80°) it formed colourless needles, m. p. 127·5°.

The following also were prepared: *nitrosonitrolanilide* of methyl-Δ^1-*cyclo*hexene, m. p. 148·5° (Found: N, 17·1. $C_{13}H_{17}O_2N_3$ requires N, 17·0%); *nitrosonitrolanilide* of α-terpineol, m. p. 144·5° (Found: N, 13·9. $C_{16}H_{23}O_3N_3$ requires N, 13·8%); *nitrosonitrolanilide* of α-pinene, m. p. 100·5° (Found: N, 14·7. $C_{16}H_{21}O_2N_3$ requires N, 14·6%); nitrosonitrol-*p*-toluidide of trimethylethylene, m. p. 155·5°; and *nitrosonitrol*-o-*toluidide* of trimethylethylene, m. p. 148° (Found: N, 18·0. $C_{12}H_{17}O_2N_3$ requires N, 17·9%). All these substances gave a definite Liebermann nitroso-reaction.

Preparation of α-Anilino-ketones.—Wallach's method (*Annalen*, 1887, **241**, 299) was used and the ketoanilide of trimethylethylene, m. p. 63°, the *ketoanilide* of methyl-Δ^1-*cyclo*hexene, m. p. 91—92° (Found: N, 6·8. $C_{13}H_{17}ON$ requires N, 6·9%), and the keto-*p*-toluidide of trimethylethylene, m. p. 98°, were prepared.

Preparation of Nitroso-α-anilino-ketones.—The method was similar to that used for the nitroso-α-anilino-ketoximes. The products, if oils, were extracted from aqueous suspension with ether, dried (anhydrous sodium carbonate), and distilled under reduced pressure. The yields were good. The *nitrosoketoanilide* of trimethylethylene, b. p. 157°/2 mm. (Found: N, 13·75. $C_{11}H_{14}O_2N_2$ requires N, 13·6%), the *nitrosoketo*-p-*toluidide* of trimethylethylene, b. p. 145°/0·8 mm. (Found: N, 12·6. $C_{12}H_{16}O_2N_2$ requires N, 12·7%) and the *nitrosoketoanilide* of methyl-Δ^1-*cyclo*hexene, m. p. 102° (Found: N, 11·9. $C_{13}H_{16}O_2N_2$ requires N, 12·0%), were prepared. All these substances gave a definite Liebermann nitroso-reaction.

Action of Alkaline β-Naphthol on α-Anilino-ketoximes and α-Anilino-ketones.—A solution of β-naphthol (0·5 g.) in 5% aqueous or alcoholic sodium hydroxide (20 ml.) was divided into two parts, to one was added the nitrosonitrolanilide of methyl*cyclo*hexene (0·1235 g.), to the other the corresponding nitrosoketoanilide (0·1160 g.), and each solution was made up to 30 ml. After 1½ hours, the first solution was brilliant red and the second faintly yellow. They were then warmed for 5 minutes at 70°; benzeneazo-β-naphthol separated from the first (aqueous) solution and no colour suggestive of an azo-dye was visible in the second. A similar comparison was made with the two types of derivatives from trimethylethylenenitrol-*p*-toluidide and trimethylethylenenitrolanilide, dyes separating from the solutions containing the ketoximes and no colour being produced in the solutions containing the ketones.

Attempted isolation of the second product of decomposition. Benzeneazo-β-naphthol having been identified, m. p. and mixed m. p. 128°, the other part of the disrupted molecule was sought. Fractional precipitation of the dye from the alcoholic reaction solution by the addition of water, followed by fractional crystallisation of the later fractions from light petroleum, yielded a colourless material. A less tedious procedure was to substitute the disodium or dipotassium salt of β-naphthol-3 : 6-disulphonic acid for β-naphthol; the soluble dye formed could then be removed from the product sought by washing with warm water or with dilute alkali. The nitrosonitrolanilide of trimethylethylene (17·3 g.), suspended in water (500 ml.) and methylated spirit (150 ml.) and treated with sodium naphtholdisulphonate (30 g.) and 20% sodium hydroxide solution (20 ml.) for 24 hours, gave, after dilution with ice-water to 1 l., 7·8 g. of product, m. p. 130—131° after recrystallisation from light petroleum (Found: C, 60·0; H, 7·7; N, 17·2; *M*, cryoscopic in benzene, 397. $C_{16}H_{24}O_3N_4$ requires C, 60·0; H, 7·5; N, 17·5%; *M*, 320).

The same *substance* is formed together with much tar by the action of alkali alone. It gives a definite Liebermann reaction, indicating the presence of a nitroso-group. It is apparently unaffected by 20% sodium hydroxide solution, with or without the addition of naphthol,

but is unstable in the presence of warm mineral or strong organic acids, decomposing with evolution of gas into neutral and basic products which have not yet been identified.

The authors' thanks are due to Miss E. Goulston for the performance of some of the micro-analyses.

THE UNIVERSITY, SYDNEY, N.S.W. [*Received, November 2nd, 1936.*]

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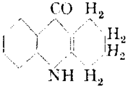
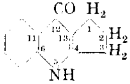
78. *The Reaction between Anthranilic Acid and* cyclo*Pentanone.*

By B. K. BLOUNT and S. G. P. PLANT.

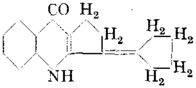
ALTHOUGH the reaction employed by Tiedtke (*Ber.*, 1909, **42**, 621) for the preparation of tetrahydroacridone (I) from anthranilic acid and *cyclo*hexanone has been applied to suberone and α-hydrindone, with the formation of the corresponding quinolones (Perkin and Plant, J., 1928, 2583; Blount, Perkin, and Plant, J., 1929, 1975), yet it was found impossible to obtain 12-keto-2 : 3 : 5 : 12-tetrahydro-β-quinindene (II) by an analogous method from *cyclo*pentanone (Blount, Perkin, and Plant, *loc. cit.*). Instead, the isolation of a small quantity of a substance, m. p. 272°, which appeared to have the formula $C_{17}H_{19}O_2N$, was



(I.)

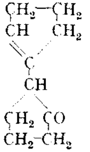


(II.)

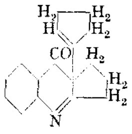


(III.)

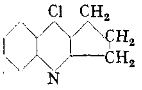
recorded, but this compound has now been obtained in much greater yields under conditions described in the experimental section, and found to melt, when pure, at 285° and possess the molecular formula $C_{17}H_{17}ON$. It therefore seemed probable that the product had resulted from the primary conversion of the *cyclo*pentanone into *cyclo*pentylidene-*cyclo*pentanone, followed by the normal Tiedtke reaction. This view was supported by the preparation of the substance from anthranilic acid and *cyclo*pentylidene*cyclo*pentanone obtained by the method of Wallach (*Ber.*, 1896, **29**, 2955), who made the significant observation that *cyclo*pentanone undergoes intermolecular condensation much more readily than *cyclo*hexanone or suberone.



(IV.)



(V.)



(VI.)

The product must be regarded as 12-*keto*-3-cyclo*pentylidene*-2 : 3 : 5 : 12-*tetrahydro*-β-*quinindene* (III), although the possibility of *cyclo*pentylidene*cyclo*pentanone reacting in the isomeric form (IV) (Dickins, Hugh, and Kon, J., 1929, 572) admits the alternative structure (V). The latter alternative was eliminated, however, by the conversion of the substance, by means of phosphorus oxychloride, into a compound derived from the replacement of hydroxyl by a single chlorine atom. Under similar conditions (II) was converted into 12-*chloro*-2 : 3-*dihydro*-β-*quinindene* (VI), but the reaction with (V) would be more complex.

EXPERIMENTAL.

12-*Keto*-3-cyclo*pentylidene*-2 : 3 : 5 : 12-*tetrahydro*-β-*quinindene*.—A mixture of equal weights (10·7 g.) of anthranilic acid and *cyclo*pentanone was gradually heated to 265°, under a reflux

air condenser, and maintained at this temperature for 10 minutes. The product was cooled, dissolved in a little hot alcohol, and poured into dilute ammonia to remove unchanged anthranilic acid. When the precipitated sticky solid was crystallised from alcohol, *12-keto-3-*cyclo*pentylidene-2 : 3 : 5 : 12-tetrahydro-β-quinindene* was obtained in yellow needles (1·9 g.), which, after recrystallisation from anisole, melted at 285°, with darkening at 263° (Found : C, 81·4; H, 6·8. $C_{17}H_{17}ON$ requires C, 81·3; H, 6·8%).

The same substance (1·5 g.; no depression in a mixed m. p.: found : C, 81·3; H, 6·9%) was obtained when a mixture of anthranilic acid (4 g.) and *cyclo*pentylidene*cyclo*pentanone (4·2 g.) was heated under similar conditions, and the product treated as before. It was insoluble in hot water, but dissolved in hot dilute hydrochloric acid, from which the hydrochloride separated, on cooling, in nearly colourless needles; the salt gave the base again on treatment with cold water.

*12-Chloro-3-*cyclo*pentylidene-2 : 3-dihydro-β-quinindene.*—A solution of the above base in ten times its weight of phosphorus oxychloride was refluxed for ½ hour, cooled, and poured into ice-water. When the yellow solid which soon separated was ground with dilute ammonia, *12-chloro-3-*cyclo*pentylidene-2 : 3-dihydro-β-quinindene* was obtained; a further quantity resulted when the aqueous solution was made alkaline. This substance separated from alcohol in almost colourless plates, m. p. 110° (Found : C, 75·5; H, 5·9; Cl, 13·1. $C_{17}H_{16}NCl$ requires C, 75·7; H, 5·9; Cl, 13·2%).

By a similar process *12-chloro-2 : 3-dihydro-β-quinindene* was obtained from 12-keto-2 : 3 : 5 : 12-tetrahydro-β-quinindene. A clear solution resulted after the reaction mixture had been left with ice-water, but the product was isolated by making this alkaline, and purified by boiling with charcoal in alcohol. It then separated from aqueous alcohol in colourless needles, m. p. 70° (Found : Cl, 17·4. $C_{12}H_{10}NCl$ requires Cl, 17·4%).

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79. *The Action of Selenium Dioxide on Sterols and Bile Acids. Part III. Cholesterol.*

By O. ROSENHEIM and W. W. STARLING.

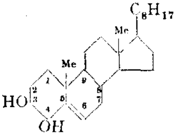
ALTHOUGH selenium dioxide reacts with ergosterol and *apo*cholic acid in alcoholic solution at room temperature (Callow and Rosenheim, J., 1933, 387; Callow, J., 1936, 462), the main reaction consisting in partial dehydrogenation, yet cholesterol is remarkably resistant to this reagent in alcoholic solution, even on boiling. Reaction, indicated by a precipitate of red selenium, takes place readily, however, when its solution in glacial acetic acid, nitrobenzene, dioxan, or acetonitrile is heated with selenium dioxide. In the first two solvents the main crystallised reaction product (yield, 35—40%) is a compound $C_{27}H_{46}O_2$, m. p. 176—177°, which was characterised as an unsaturated diol. Its constitution as a cholestene-α-glycol, *viz.*, cis-$\Delta^{5:6}$-*cholestene-3 : 4-diol* (I), was established by the following evidence :

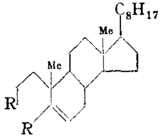
(1) The presence of a single ethenoid linkage was demonstrated by (*a*) quantitative perbenzoic acid titration and preparation of a saturated *monoxide*, $C_{27}H_{46}O_3$, m. p. 173—174°; (*b*) bromine titration; and (*c*) catalytic reduction with Adams's catalyst to cis-*cholestane-3 : 4-diol*, $C_{27}H_{48}O_2$, m. p. 202—203° (reduction with a palladium catalyst yields a mixture of cholestane, coprostane, and cholestan-3-ol). (2) Evidence accounting for the functions of the two oxygen atoms is afforded by the preparation of various mono-, di-, and mixed esters, proving that the compound is a disecondary alcohol. (3) The relative position of the hydroxyl groups and their function as a disecondary α-glycol follow from the results of quantitative titration with lead tetra-acetate by Criegee's method (*Ber.*, 1931, **64**, 260). The unsaturated dialdehyde, $C_{27}H_{44}O_2$ (II, R = CHO), resulting on oxidation of the diol with lead tetra-acetate, was characterised by its *di-*o*-tolylsemicarbazone* (and other derivatives), and furnished on further oxidation with hydrogen peroxide an unsaturated dicarboxylic acid, $C_{27}H_{44}O_4$, m. p. 292—293° (II, R = CO_2H). The same acid was also obtained on oxidation of the diol with potassium hypobromite, and was found to be identical with Diels's acid (Diels and Abderhalden, *Ber.*, 1903, **36**, 3179; 1904, **37**, 3092). Further,

the action of lead tetra-acetate on the saturated diol $C_{27}H_{48}O_2$ and oxidation of the product with hydrogen peroxide yielded the saturated acid $C_{27}H_{46}O_4$, characterised by its dimethyl ester, and identical with the saturated Diels's acid (Windaus, *Ber.*, 1919, **52**, 170). This fact incidentally furnishes evidence that, in the saturated diol, addition of hydrogen at C_5 had occurred in the *trans*-position relative to the 10-methyl group.

These observations prove that selenium dioxide attacks the cholesterol molecule mainly at the CH_2 group situated between the 5 : 6 ethenoid linkage and the secondary alcohol group at C_3. No evidence for hydroxylation at C_7 or for ketone formation was obtained.

(I.)





(II.)

The diol is quantitatively precipitated by digitonin in alcoholic solution. The digitonide, m. p. 240—242°, contains its constituents in equimolecular proportion, like cholesterol digitonide. The mono-esters, formed by the 3-hydroxyl group, are not precipitable by digitonin, thus proving that the 4-hydroxyl group does not combine with digitonin (cf. Tschesche and Hagedorn, *Ber.*, 1935, **68**, 2247). Characteristic blue colour reactions are given by the substance with arsenic trichloride, trichloroacetic acid, and by sulphuric acid or zinc chloride in glacial acetic acid. In the Salkowski reaction the chloroform layer is blue, and the sulphuric acid layer red with a green fluorescence. The glycol distils without decomposition in a high vacuum.

As was to be expected, the presence of the α-glycol group confers great reactivity upon this derivative of cholesterol, the first of its type. For instance, it rapidly loses one molecule of water on warming with dilute mineral acids, yielding a ketone and a compound $C_{27}H_{46}O_2$ (?), m. p. 139—140°, which is being investigated. The ketone was identified as coprostenone (cholestenone) by its characteristic *o-tolylsemicarbazone*. With Brady's reagent no reaction takes place at room temperature, but on warming, the 2 : 4-dinitrophenylhydrazone of coprostenone rapidly crystallises.

It is somewhat surprising that the action of selenium dioxide on the esters of cholesterol (the acetate and benzoate have so far been examined) proceeds in a different direction from that on cholesterol itself. In the case of the acetate, a small percentage only of the monoacetate of the *cis*-diol can be isolated, the main crystallised reaction product (yield 25—30%) being the *diacetate*, m. p. 135—136°, of the isomeric trans-$\Delta^{5:6}$-*cholestene*-3 : 4-*diol*, $C_{27}H_{46}O_2$, m. p. 257—258°. Cholesteryl benzoate in glacial acetic acid solution yields on oxidation with selenium dioxide a mixture in about equal proportions of the monobenzoate of the *cis*-diol with a compound, m. p. 128—129°. The latter, a *cholestene*-3 : 4-*diol* 3-*benzoate*-4-*acetate*, $C_{36}H_{52}O_4$, gives on hydrolysis the *trans*-diol, m. p. 257—258°. The preferential acetylation of the 4-hydroxyl group in the *trans*-diol is analogous to the behaviour of the monobenzoate of *trans-cyclo*hexane-1 : 2-diol, which reacts more readily with nitrobenzoyl chlorides than the benzoate of the corresponding *cis*-diol (Wilson and Read, J., 1935, 1269).

The constitution of the *trans*-diol was established by the same methods as in the case of its isomeride. That it contains a single ethenoid linkage follows from the results of (*a*) titration with bromine and preparation of the *dibromide* $C_{27}H_{46}O_2Br_2$, and (*b*) titration with perbenzoic acid and isolation of the saturated trans-*cholestanediol oxide*, $C_{27}H_{46}O_3$, m. p. 164—165°. Catalytic reduction (platinum oxide) yields trans-*cholestane*-3 : 4-*diol*, $C_{27}H_{48}O_2$, m. p. 194—195°. On heating with dilute mineral acids, the *trans*-diol rapidly loses one molecule of water and yields coprostenone (cholestenone), like its isomeride. It gives intense blue colours with various sterol reagents and is precipitable by digitonin like the *cis*-diol, but it differs from the latter by its sparing solubility in most organic solvents. This relative insolubility enabled us (*Chem. and Ind.*, 1933, **52**, 1056) to recognise the *trans*-diol

as a constituent of the resinous product called "Oxycholesterol" by Lifschütz (*Z. physiol. Chem.*, 1919, **106**, 279), which is obtained from cholesterol dibromide by debromination with sodium acetate.

The assignation of the respective configurations to the two isomeric α-glycols is based on the difference in the speed of their reaction with lead tetra-acetate (Criegee, Kraft, and Rank, *Annalen*, 1933, **507**, 159). The action of this reagent on the diol, m. p. 177°, is extremely rapid (reaction velocity $k_{20^\circ} = 51{\cdot}1$), but the diol, m. p. 258°, reacts so slowly that accurate determinations of its reaction velocity were not attempted. These results, in agreement with the melting point rule, justify the alternative designation of the two α-glycols as *cis-cis-* and *cis-trans-*$\Delta^{5:6}$-cholestene-3 : 4-diol respectively—the nomenclature refers to the 3- and 4-hydroxyl group as *cis* or *trans* relative to the 10-methyl group (cf. Schoenheimer and Evans, *J. Biol. Chem.*, 1936, **114**, 571; Callow and Young, *Proc. Roy. Soc.*, 1936, *A*, **157**, 195). Measurements of the surface films of the diols and their diacetates were kindly carried out by Dr. Askew, the results agreeing with the above conclusions (Adam, Askew, and Danielli, *Biochem. J.*, 1935, **29**, 1786).

The ease with which these primary oxidation products of cholesterol are converted by loss of water into coprostenone, readily reducible to coprostanone and coprostanol *in vitro*, makes them of considerable biochemical interest in connection with the conversion by the animal organism of cholesterol into coprostanol. This conversion involves a reduction of the 5 : 6 ethenoid linkage. Although the animal organism is known to effect the reduction of cholesterol to cholestanol (the *trans*-decalin derivative), the mechanism of the conversion into coprostanol, the *cis*-isomeride, has remained hitherto unexplained (for a recent discussion of the problem, see Gardner, Gainsborough, and Murray, *Biochem. J.*, 1935, **29**, 1139). The unusual reactivity of the cholestene-α-glycols and their easy conversion into coprostenone suggested that they, and not cholesterol itself, are the immediate precursors of coprostanol, produced subsequently by intestinal bacterial reduction. On the assumption that primary oxidation to one of the α-glycols may play a rôle in cholesterol metabolism, feeding experiments with the above-described substances were undertaken (Rosenheim and Webster, *Nature*, 1935, **136**, 474). A large increase in the excretion by rats of fæcal coprostanol was observed after the administration of coprostenone, and a distinct effect was obtained with the *cis*-diol, whereas the *trans*-diol was without action, being excreted unchanged. Similar results with coprostenone were obtained simultaneously by Schoenheimer, Rittenberg, and Graf (*J. Biol. Chem.*, 1935, **111**, 183), who made use also of deuterium as an indicator.

EXPERIMENTAL.

cis-$\Delta^{5:6}$-*Cholestene*-3 : 4-*diol and its Derivatives.*

A solution of selenium dioxide (25 g.) in water (10 c.c.), to which glacial acetic acid (500 c.c.), warmed to 80°, has been added, is rapidly mixed with a solution of cholesterol (50 g.) in benzene (250 c.c.), also warmed to 80°. The mixture, which rapidly turns yellow and then red, is refluxed on a steam-bath for 1 hour. After the addition of sodium acetate (crystals, 100 g.), and heating for a few minutes, the black modification of selenium is deposited and removed. The filtrate is poured into half-saturated salt solution (1 l.), the benzene layer separated, washed with water, and dried over sodium sulphate, and the solvent removed under reduced pressure. The residue (60 g.) is suspended in light petroleum (b. p. 40—50°; 1500 c.c.), allowed to settle in a tall stoppered cylinder, and washed twice with the same solvent by decantation. The crude, creamy-white product (26 g.), m. p. 174—175°, is crystallised once from acetone (norit) and from 85% alcohol, from which the cis-*diol* (20 g.) separates in inch-long monoclinic needles, m. p. 176—177°, b. p. 255—260°/0·2 mm., $[\alpha]_D^{20^\circ}$ − 60·0°, $[\alpha]_{5461}^{20^\circ}$ − 71·0° (*c*, 1·566*); $\alpha_{5461}/\alpha_D = 1{\cdot}19$ (Found: † C, 80·4; H, 11·3. $C_{27}H_{46}O_2$ requires C, 80·5; H, 11·5%). The diol gives an intense blue coloration with the trichloroacetic acid reagent (Rosenheim, *Biochem. J.*, 1929, **23**, 47).

The *diacetate*, prepared by refluxing the *cis*-diol (1 g.) with acetic anhydride (10 c.c.) for 1 hour, crystallised in needles on cooling, and was recrystallised from spirit; m. p. 169—170°, $[\alpha]_D^{23^\circ}$ − 96·1°, $[\alpha]_{5461}^{23^\circ}$ − 117·1° (*c*, 1·576); $\alpha_{5461}/\alpha_D = 1{\cdot}20$ (Found: C, 76·3; H, 10·4. $C_{31}H_{50}O_4$

* The optical rotations were measured in a 4-dm. tube; all solutions were in chloroform unless otherwise stated.

† Micro-analyses by Dr. G. Weiler, Oxford.

requires C, 76·5; H, 10·4%). Hydrolysis of the diacetate with sodium ethoxide yielded the *cis*-diol. The diacetate gives blue colour reactions with trichloroacetic acid, as well as with antimony trichloride in chloroform. In acetic acid solution the free diol also gives a blue colour on warming with the antimony trichloride reagent, whereas it does not react in chloroform solution, remaining colourless for some time and turning reddish-purple only after some hours.

cis-*Cholestene*-3 : 4-*diol* 3-*benzoate* is conveniently prepared by boiling for 5 minutes a solution of cholesteryl benzoate (10 g.) in glacial acetic acid (100 c.c.) with a solution of selenium dioxide (2 g.) in water (1 c.c.), to which glacial acetic acid (100 c.c.) has been added. Sodium acetate (crystals, 7·5 g.) is added, and the black deposit of selenium removed. On cooling, the crude monobenzoate (3·8 g.) crystallises, and is recrystallised from methyl alcohol–ethyl acetate; needles, m. p. 209—210°, not melting to an anisotropic liquid; $[\alpha]_D^{20°}$ − 30·7°, $[\alpha]_{5461}^{33°}$ − 36·9° (*c*, 0·758); α_{5461}/α_D = 1·20 (Found: C, 80·7; H, 10·0. $C_{34}H_{50}O_3$ requires C, 80·6; H, 9·9%). Hydrolysis furnished the *cis*-diol. The 3-monobenzoate is also obtained from the *cis*-diol in pyridine by treatment with benzoyl chloride (1 equiv.) at room temperature.

cis-*Cholestenediol* 3-*benzoate*-4-*acetate*, prepared from the 3-benzoate by refluxing with acetic anhydride, crystallises in plates, m. p. 166—167°, $[\alpha]_D^{20°}$ − 55·9°, $[\alpha]_{5461}^{20°}$ − 66·6° (*c*, 1·667); α_{5461}/α_D = 1·19 (Found: C, 78·8; H, 9·5. $C_{36}H_{52}O_4$ requires C, 78·7; H, 9·6%). The *dibenzoate*, obtained by heating the diol in dry pyridine with slightly more than the calculated amount of benzoyl chloride for 5 hours on the water-bath, crystallises from alcohol in prismatic needles, m. p. 150—151°, $[\alpha]_D^{23°}$ − 53·9°, $[\alpha]_{5461}^{23°}$ − 63·5° (*c*, 0·835), α_{5461}/α_D = 1·18 (Found: C, 80·4; H, 8·8. $C_{41}H_{54}O_4$ requires C, 80·6; H, 8·9%). The *bis*-3 : 5-*dinitrobenzoate*, prepared by the pyridine method, crystallises in yellowish plates, m. p. 220—221°, $[\alpha]_D^{22°}$ − 39·6°, $[\alpha]_{5461}^{22°}$ − 45·5° (*c*, 1·054), α_{5461}/α_D = 1·15 (Found: C, 62·3; H, 6·5. $C_{41}H_{50}O_{12}N_4$ requires C, 62·3; H, 6·4%).

Perbenzoic acid titration. After 48 hours at 0°, 0·1030 g. of *cis*-diol consumed the equivalent of 3·86 mg. of oxygen, corresponding to 0·94 ethylenic linkage, and after 100 hours 0·1000 g. absorbed 3·93 mg. (0·98 ethylenic linkage).

cis-*Cholestane*-3 : 4-*diol Oxide*.—The *cis*-diol (4 g.) in chloroform (200 c.c.) was kept at 0° with a solution of perbenzoic acid (1·1 atoms of O) in chloroform (20 c.c.). The reaction was complete after 70 hours. The solution, after washing with aqueous sodium carbonate and water, was dried over sodium sulphate, and the solvent removed. The *oxide* was crystallised from spirit and from acetone, separating in slender needles, m. p. 173—174°, $[\alpha]_D^{19°}$ + 3·9°, $[\alpha]_{5461}^{19°}$ + 4·5° (*c*, 1·142); α_{5461}/α_D = 1·15 (Found: 77·7; H, 11·1. $C_{27}H_{46}O_3$ requires C, 77·4; H, 11·1%). The oxide gave no coloration either with tetranitromethane in chloroform or with trichloroacetic acid. In the Salkowski test it behaves like cholesteryl oxide (colourless chloroform layer, red acid layer; cf. Westphalen, *Ber.*, 1915, **48**, 1064). The *diacetate* of the *cis*-diol oxide, prepared by acetylation with acetic anhydride, separated from methyl alcohol in clusters of needles, m. p. 178—179°; $[\alpha]_D^{19°}$ − 22·1°, $[\alpha]_{5461}^{19°}$ − 27·5° (*c*, 0·610); α_{5461}/α_D = 1·25 (Found: C, 74·1; H, 9·8. $C_{31}H_{50}O_5$ requires C, 74·0; H, 10·0%). On admixture with the oxide (m. p. 174°), a m. p. depression of 35° was observed.

Bromine titration (by the pyridine sulphate dibromide method). After 5 minutes at room temperature, 0·1054 g. of the *cis*-diol absorbed 40·3 mg. bromine (0·96 ethylenic linkage), and after 30 minutes, 0·0510 g. absorbed 20·8 mg. (1·02 ethylenic linkages).

cis-*Cholestene*-3 : 4-*diol dibromide*. Solutions of the *cis*-diol (5 g.) in chloroform (15 c.c.) and of bromine (0·66 c.c.) in acetic acid (120 c.c.) are rapidly mixed. Crystallisation of the *dibromide* begins after about one minute, and is completed by cooling in ice. The product (4·2 g.), m. p. 95—97°, rapidly decomposes on recrystallisation from hot solvents, but may be recrystallised from chloroform–acetic acid at room temperature, giving prismatic needles, m. p. 110—112° (decomp.) (Found: C, 57·5; H, 8·3. $C_{27}H_{46}O_2Br_2$ requires C, 57·6; H, 8·2%).

The dibromide is rapidly debrominated on mixing its solution in benzene with a solution of sodium iodide in alcohol at room temperature (cf. Schoenheimer, *J. Biol. Chem.*, **1935**, **110**, 461), yielding the *cis*-diol. A solution of the dibromide in acetone rapidly turns yellow on warming, and gives off hydrogen bromide. On cooling, a neutral bromine-free substance, m. p. 133—134°, crystallises out; this is *isopropylidene cholestene*-3 : 4-*diol*, $[\alpha]_D$ − 38·2°, $[\alpha]_{5461}$ − 46·9° (*c*, 1·406); α_{5461}/α_D = 1·23 (Found: C, 81·4; H, 11·4. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·7%), also obtained from the *cis*-diol and acetone containing 1% of hydrogen chloride. The *trans*-diol does not yield an acetone compound, a fact supplying additional evidence for the assignation of the *cis*- and the *trans*-configuration to the respective isomeric α-glycols.

Hydrogenation. A suspension of platinum oxide (0·45 g.) in acetic acid (40 c.c.) was reduced with hydrogen, a solution of the *cis*-diol (10 g.) in acetic acid (300 c.c.) then added, and the whole shaken with hydrogen. Absorption took place rapidly and was complete in 2½ hours. Nearly

2 mols. of hydrogen were absorbed, no break in the absorption curve being noticeable after the addition of 2 atoms. A crystalline precipitate was dissolved by warming, the catalyst removed, and the solution concentrated under reduced pressure until crystallisation began. The crude product (6·5 g.) was dissolved in ether, in which it is sparingly soluble, by extraction (Soxhlet) and crystallised in the extraction flask, m. p. 193—194°. Crystallisation from heptane and from acetone yielded shiny leaflets of cis-*cholestane*-3 : 4-*diol*, m. p. 202—203°, $[\alpha]_D^{24°}$ + 18·8°, $[\alpha]_{5461}^{24°}$ + 22·2° (*c*, 1·206); α_{5461}/α_D = 1·18 (Found : C, 80·4; H, 12·0. $C_{27}H_{48}O_2$ requires C, 80·1; H, 12·0%). The *diacetate*, obtained by refluxing the saturated diol with acetic anhydride, crystallised from methyl alcohol in long needles, m. p. 136—137°, $[\alpha]_D^{22°}$ − 7·1° (*c*, 1·0) (Found : C, 76·3; H, 10·8. $C_{31}H_{52}O_4$ requires C, 76·2; H, 10·7%).

After removal of the saturated diol, the mother-liquors were precipitated with digitonin in alcoholic solution. The digitonide was dissolved in pyridine, the digitonin precipitated with ether and removed. The residue of the ethereal filtrate yielded cholestan-3-ol, crystallising in triclinic plates, m. p. 141—142°, unchanged after admixture with an authentic specimen (Found : C, 79·6; H, 12·4. Calc. for $C_{27}H_{48}O,H_2O$: C, 79·7; H, 12·4%). The mixture of hydrocarbons, not precipitated by the above digitonin treatment, was recovered and separated by fractional crystallisation. The least soluble fraction furnished cholestane, crystallising in monoclinic plates, m. p. 80—81°, not depressed in admixture with authentic cholestane (Found : C, 87·0; H, 13·0. Calc. for $C_{27}H_{48}$: C, 87·0, H, 13·0%). From the more soluble fractions, small amounts of coprostane were obtained, crystallising in orthorhombic needles, m. p. and mixed m. p. 70—71° (Found : C, 87·0; H, 13·0. Calc. for $C_{27}H_{48}$: C, 87·0; H, 13·0%).

When the diacetate of the *cis*-diol was catalytically reduced over palladised charcoal in neutral or acetic acid solution, rapid absorption of nearly 3 mols. of hydrogen took place, yielding a mixture of cholestane and coprostane. The same catalyst acting on the *cis*-diol in alcoholic solution furnished cholestan-3-ol in addition to the hydrocarbons. The constituents of the mixtures were separated and identified as described above. In no instance was the saturated *cis*-diol obtained by the use of a palladium catalyst.

Lead tetra-acetate titration. After 24 hours at room temperature, 0·1046 g. of *cis*-diol consumed 5·08 c.c. of *N*/10-lead tetra-acetate, corresponding to 0·97 atom of oxygen, and after 48 hours, 0·1030 g. consumed 5·22 c.c. (1·02 atoms of O).

*Di-*o*-tolylsemicarbazone of dialdehyde*, $C_{27}H_{44}O_2$. A solution of lead tetra-acetate (2·5 g.) in acetic acid (100 c.c.) is added to a suspension of the *cis*-diol (1 g.) in acetic acid (50 c.c.). The clear solution resulting after 2 minutes' shaking is kept for 24 hours at room temperature. The crude dialdehyde (0·9 g.), obtained on extraction of the reaction mixture with light petroleum as a colourless oil, is dissolved in alcohol (10 c.c.). A solution of *o*-tolylsemicarbazide (1 g.) (cf. Lei, Sak, and Shih, *J. Chinese Chem. Soc.*, 1935, **3**, 247) in hot spirit (20 c.c.) and 5 drops of acetic acid are added. Crystallisation begins within 10 minutes. After two recrystallisations from alcohol, the *di-*o*-tolylsemicarbazone* is obtained in clusters of needles, m. p. 192—193° (Found : C, 74·7; H, 9·1; N, 12·4. $C_{43}H_{62}O_2N_6$ requires C, 74·4; H, 8·9; N, 12·1%). The *bis*-2 : 4-*dinitrophenylhydrazone*, prepared from the crude dialdehyde by means of Brady's reagent, crystallised from benzene as a microcrystalline crimson powder (Found : N, 14·7. $C_{39}H_{52}O_8N_8$ requires N, 14·7%). The *disemicarbazone*, obtained in the usual way, was purified by digestion with boiling alcohol; m. p. 218—219° (Found : N, 16·5. $C_{29}H_{50}O_2N_6$ requires N, 16·4%).

Oxidation of Dialdehyde, $C_{27}H_{44}O_2$, *to Diels's Acid.*—Hydrogen peroxide (100-vol., 0·5 c.c.) is added to a solution of the aldehyde (1·0 g.) in acetic acid (5 c.c.). An addition product, m. p. 121—122°, crystallises out, which dissolves on warming. The solution is kept on a steam-bath for 2 hours, crystallisation of the acid starting after ½ hour's heating. After recrystallisation from acetic acid and methyl ethyl ketone, Diels's acid is obtained in typical tetragonal crystals, m. p. 292—293°, not depressed in admixture with authentic acid prepared from cholesterol (Found : C, 74·9; H, 10·1. Calc. for $C_{27}H_{44}O_4$: C, 75·0; H, 10·2%. 0·1130 G. required 5·4 c.c. of *N*/10-KOH for neutralisation. Calc. : 5·5 c.c.). The monomethyl ester crystallises in plates, m. p. 125—126°, alone or in admixture with an authentic specimen (0·1034 g. required 2·3 c.c. *N*/10-KOH. Calc. : 2·3 c.c.).

Diels's acid was also obtained by shaking the finely powdered *cis*-diol (5 g.) for 20 hours with a solution of potassium hypobromite, prepared by adding bromine (3 c.c.) to a mixture of ice (40 g.) and potassium hydroxide (25%, 50 c.c.). The acid and its mono-methyl and -ethyl esters were identified by mixed m. p.'s with authentic specimens and by elementary analyses.

These observations are consistent with the view that both *cis*-cholestenediol and the dialdehyde $C_{27}H_{44}O_2$ are intermediate products in the oxidation of cholesterol by potassium hypobromite to Diels's acid (Diels and Abderhalden, *loc. cit.*).

Dihydro-Diels's Acid from cis-*Cholestane-3 : 4-diol.*—After 40 hours, 0·2078 g. of the saturated *cis*-diol consumed 10·27 c.c. of *N*/10-lead tetra-acetate, corresponding to 1·0 atom of oxygen. The saturated dialdehyde was extracted from the reaction mixture with ether, and oxidised with hydrogen peroxide in acetic acid solution. The resulting acid crystallised from acetic acid in leaflets, m. p. 248—250° (Found : C, 74·6; H, 11·0. Calc. for $C_{27}H_{46}O_4$: C, 74·6; H, 10·7%). The dimethyl ester, prepared with diazomethane, crystallised from methyl alcohol in prisms, m. p. 125—126° (Found : C, 75·6; H, 10·9. Calc. for $C_{29}H_{50}O_4$: C, 75·3; H, 10·9%). The m. p.'s of the acid and of its dimethyl ester are given by Windaus (*Ber.*, 1919, **52**, 175) as 252° and 123—124° respectively, whilst the isomeric acid, m. p. 249°, from coprosterol yields a dimethyl ester, m. p. 61° (*idem*, *Ber.*, 1916, **49**, 1732).

Digitonin Precipitation.—A solution of the *cis*-diol (542 mg.) in boiling spirit (8 c.c.) was mixed with a 1% solution of digitonin in hot 90% alcohol (30 c.c.). The digitonide separated on cooling in starry aggregates of needles. After 24 hours at 0°, the precipitate was collected, washed with 90% alcohol and with ether, dried at 100°, and weighed. Yield of digitonide, 0·2108 g., m. p. 240—242° (decomp.). Like cholesterol digitonide, it contains one-quarter of its weight of sterol (Windaus, *Z. physiol. Chem.*, 1910, **65**, 112), which is recovered nearly quantitatively by the pyridine–ether method (Schoenheimer and Dam, *ibid.*, 1933, **215**, 59).

Coprostenone (*Cholestenone*) *from* cis-*Cholestenediol.*—(a) A solution of the *cis*-diol (2·5 g.) in acid alcohol (180 c.c., containing 7 c.c. of concentrated hydrochloric acid) is heated for 10 minutes on a water-bath. After the addition of potassium acetate (8 g.), the solution is cooled and the precipitated potassium chloride removed. A solution of *o*-tolylsemicarbazide (2 g.; see p. 381). in hot alcohol (20 c.c.) is added. *Coprostenone*-o-*tolylsemicarbazone* crystallises from butyl alcohol in feathery needles, m. p. 243—244°, alone or in admixture with an authentic specimen (Found : N, 8·0. $C_{35}H_{53}ON_3$ requires N, 8·0%). A solution of the *cis*-diol (0·2 g.) in acid alcohol (15 c.c., containing 0·6 c.c. of concentrated hydrochloric acid) is added to a suspension of 2 : 4-dinitrophenylhydrazine (0·1 g.) in alcohol (10 c.c.). After warming on a water-bath a voluminous brick-red precipitate is formed within a few minutes. Coprostenone-2 : 4-dinitrophenylhydrazone (cf. Ralls, *J. Amer. Chem. Soc.*, 1933, **55**, 2092) separates from benzene–alcohol as a woolly mass of hair-like crystals, which change into stout transparent prisms on standing, m. p. 233—234°, not depressed in admixture with an authentic specimen (Found : C, 70·0; H, 8·9; N, 10·2. Calc. for $C_{33}H_{48}O_4N_4$: C, 70·2; H, 8·6; N, 10·0%). The same reaction takes place on warming a solution of the *cis*-diol with Brady's reagent (J., 1931, 756) and may be used to demonstrate the formation of coprostenone from the *cis*-diol at body temperature in an incubator.

(b) Coprostenone, m. p. 80—81°, alone or admixed with an authentic specimen, was obtained by heating the semicarbazone, m. p. 233—234° (0·9 g., prepared from the *cis*-diol as above by means of semicarbazide acetate), with a mixture (50 c.c.) of acetic and hydrochloric acids (1 : 1) for 30 minutes on a water-bath (Found : C, 84·4; H, 11·3. Calc. for $C_{27}H_{44}O$: C, 84·3; H, 11·5%). Coprostenone was also isolated and identified by the usual methods from the reaction products obtained by heating the finely-powdered *cis*-diol (1 g.) with water (10 c.c.) in a sealed tube to 200° for 8 hours.

trans-$\Delta^{5:6}$-*Cholestene-3 : 4-diol and its Derivatives.*

Hot solutions of cholesteryl acetate (20 g.) and selenium dioxide (10 g., 5 c.c. water), each in 200 c.c. of acetic acid, are mixed and boiled for 5 minutes. After the addition of sodium acetate (crystals, 60 g.), the mixture is reheated and the black deposit of selenium removed. The cooled filtrate, to which ether (200 c.c.) has been added, is poured into half-saturated salt solution (1 l.). The ethereal layer is separated, washed with water, dried over sodium sulphate, and the solvent removed. The resinous reddish residue contains a mixture (which may be separated by appropriate selective solvents) of the mono- and the di-acetates of the *cis*- and the *trans*-diol. Acetylation is completed by refluxing the resin with acetic anhydride for ½ hour. The crystals, which separate on cooling, are removed, dried over soda–lime in a desiccator, and washed with spirit (60 c.c.) by grinding in a mortar. The crude diacetates (10·8 g.) are hydrolysed by boiling their solution in methyl alcohol (300 c.c.) with 5% methyl-alcoholic sodium methoxide (120 c.c.). Crystallisation of the *trans*-diol begins after a few minutes and is complete in ½ hour. The diol is sparingly soluble in light petroleum, ether, alcohol, ethyl acetate, etc., but may be recrystallised from nitrobenzene, dioxan, or pyridine. Purification of the crude product (5 g., m. p. 256—257°) is preferably effected by acetylation, recrystallisation of the diacetate, and subsequent hydrolysis. trans-*Cholestene-3 : 4-diol* crystallises in orthorhombic needles, m. p. 257—258°, b. p. 255—260°/0·2 mm., $[\alpha]_D^{20°}$ + 6·0°, $[\alpha]_{5461}^{20°}$ + 7·5° (*c*, 0·50 in pyridine); α_{5461}/α_D = 1·25 (Found : C, 80·6; H, 11·6. $C_{27}H_{46}O_2$ requires C, 80·5; H, 11·5%).

trans-*Cholestene*-3 : 4-*diol diacetate*, prepared by refluxing the *trans*-diol with acetic anhydride, crystallised from methyl alcohol in long needles, m. p. 135—136°, $[\alpha]_D^{18°}$ − 13·3°, $[\alpha]_{5461}^{18°}$ − 16·4° (*c*, 1·11); α_{5461}/α_D = 1·23 (Found: C, 76·3; H, 10·2. $C_{31}H_{50}O_4$ requires C, 76·5; H, 10·4%). The *dibenzoate*, prepared by the pyridine method, crystallises in prismatic needles, m. p. 181—182°, $[\alpha]_D^{20°}$ − 74·4°, $[\alpha]_{5461}^{20°}$ − 91·4° (*c*, 1·35); α_{5461}/α_D = 1·23 (Found: C, 80·7; H, 9·0. $C_{41}H_{54}O_4$ requires C, 80·6; H, 8·9%). The 3-*benzoate*-4-*acetate* is obtained, together with the monobenzoate of the *cis*-diol, when cholesteryl benzoate is treated with selenium dioxide in acetic acid solution. The filtrate from *cis*-cholestene-3 : 4-diol 3-benzoate (see above) is poured into water, and the granular precipitate taken up in light petroleum. After removal of the solvent and repeated crystallisation of the residue from chloroform–methyl alcohol and from spirit, the mixed ester crystallises in prisms, m. p. 128—129°, $[\alpha]_D^{20°}$ − 21·2°, $[\alpha]_{5461}^{20°}$ − 26·2° (*c*, 1·448); α_{5461}/α_D = 1·23 (Found: C, 78·8; H, 9·5. $C_{36}H_{52}O_4$ requires C, 78·7; H, 9·6%). On hydrolysis in ethereal solution with sodium ethoxide, the ester yielded the *trans*-diol.

Perbenzoic acid titration. Suspensions of the *trans*-diol (50 mg.) in chloroform (5 c.c.), kept at 0° and titrated after 48, 96, and 120 hours, absorbed amounts of oxygen corresponding to 0·88, 0·94, and 0·98 ethylenic linkage respectively.

trans-*Cholestane*-3 : 4-*diol Oxide*.—A suspension of the *trans*-diol (2 g.) in chloroform (200 c.c.), mixed with a solution of perbenzoic acid (1·1 atoms of O) in chloroform, was kept at 0° for 9 days, the reaction then being complete. The *oxide* was isolated as described for that of the *cis*-diol, and crystallised from acetone in long needles, m. p. 164—165°, $[\alpha]_D^{20°}$ − 7·5°, $[\alpha]_{5461}^{20°}$ − 9·2° (*c*, 0·648); α_{5461}/α_D = 1·23 (Found: C, 77·5; H, 10·7. $C_{27}H_{46}O_3$ requires C, 77·4; H, 11·1%). Its *diacetate* crystallises from methyl alcohol in rhombic plates, m. p. 154—155°, $[\alpha]_D^{19°}$ − 58·5°, $[\alpha]_{5461}^{19°}$ − 69·6° (*c*, 1·028); α_{5461}/α_D = 1·19 (Found: C, 74·0; H, 9·9. $C_{31}H_{50}O_5$ requires C, 74·0; H, 10·0%).

Bromine titration (by the pyridine sulphate dibromide method). After 30 minutes at room temperature, 0·1000 g. of the *trans*-diol absorbed 44·2 mg. of bromine, corresponding to 1·1 ethylenic linkages.

trans-*Cholestene*-3 : 4-*diol dibromide*. A suspension of the *trans*-diol (1 g.) in chloroform (100 c.c.) was shaken for 1 hour with pyridine sulphate dibromide solution (200 c.c.). The excess of bromine was removed with *N*/10-sodium thiosulphate, the chloroform layer separated, washed with water and with sodium carbonate solution. After drying over sodium sulphate, the solvent was removed under reduced pressure, and the residue crystallised repeatedly from alcohol or acetone. The *dibromide* crystallises in fine needles from benzene, m. p. 196—197° (decomp.) (Found: C, 57·7; H, 7·9; Br, 28·8. $C_{27}H_{46}O_2Br_2$ requires C, 57·7; H, 8·2; Br, 28·5%).

Unlike the dibromide of the *cis*-diol, that of the *trans*-diol is remarkably stable. Whereas the former is instantly debrominated by sodium iodide at room temperature, the latter is recovered unchanged after 5 hours' boiling of its benzene solution with an alcoholic solution of sodium iodide. On boiling in alcoholic solution for 2 hours with zinc dust, however, bromine is removed and the *trans*-diol is recovered.

Hydrogenation. On account of the insolubility of the *trans*-diol, the more soluble diacetate (10 g.) in ether–acetic acid solution was catalytically reduced with platinum oxide (0·47 g.) under the same conditions as for the *cis*-diol (see above). Again, nearly 2 mols. of hydrogen were rapidly absorbed (1 hour) without any break in the absorption curve. After removal of the catalyst and evaporation of the ether, a semicrystalline waxy deposit (1·9 g.), consisting mainly of cholestane, was removed. The solution was diluted with water and extracted with ether. After removal of the solvent, the residue (6·5 g.) was fractionally crystallised from methyl alcohol and separated into two main fractions. The least soluble fraction, m. p. 192—193°, was crystallised from benzene–petrol and finally from acetone, yielding stout hexagonal plates of trans-*cholestane*-3 : 4-*diol*, m. p. 194—195°, $[\alpha]_D^{20°}$ + 10·2°, $[\alpha]_{5461}^{20°}$ + 12·1° (*c*, 1·184); α_{5461}/α_D = 1·16 (Found: C, 80·0; H, 12·1. $C_{27}H_{48}O_2$ requires C, 80·1; H, 12·0%). The *diacetate*, prepared by refluxing with acetic anhydride, crystallised in thin plates, m. p. 140—141° (Found: C, 76·4; H, 10·8. $C_{31}H_{52}O_4$ requires C, 76·2; H, 10·7%).

The diol gave no coloration either with trichloroacetic acid or with tetranitromethane in chloroform. After 48 hours' treatment with lead tetra-acetate, no measurable consumption of oxygen took place, and the *trans*-diol was recovered unchanged.

Cholestane and cholestan-3-ol were isolated, and identified by the usual methods, from the more soluble fractions of the reduction products. Catalytic reductions of the *trans*-diol diacetate over palladium catalysts yielded in every instance a mixture of cholestane, coprostane, and cholestan-3-ol, in the same proportions as in the case of the *cis*-diol described above.

Coprostenone (*Cholestenone*) *from* trans-*Cholestene*-3 : 4-*diol*.—A suspension of the *trans*-

diol (0·5 g.) in alcohol (30 c.c., containing 1·5 c.c. of concentrated hydrochloric acid) is refluxed for 10 minutes on a water-bath and treated with *o*-tolylsemicarbazide (see above), yielding *coprostenone*-o-*tolylsemicarbazone*, m. p. 243—244° (Found: N, 8·1. $C_{35}H_{53}ON_3$ requires N, 8·0%). After removal of the tolylsemicarbazone, the filtrate yielded a compound $C_{27}H_{46}O_2$(?), m. p. 139—140°, which is being investigated. A mixture with the substance of the same m. p., obtained under similar conditions from the *cis*-diol, showed no depression of m. p.

Coprostenone-2 : 4-dinitrophenylhydrazone, m. p. 233—234° (Found: N, 10·1. $C_{33}H_{48}O_4N_4$ requires N, 10·0%), was obtained by adding Brady's reagent (5 c.c.) to a suspension of the *trans*-diol (0·5 g.) in alcohol (25 c.c.) and heating for a short time on a water-bath. The *semicarbazone*, m. p. 233—234° (Found: N, 9·5. $C_{28}H_{47}ON_3$ requires N, 9·5%), prepared from the *trans*-diol as above by means of semicarbazide acetate, was heated with a mixture of acetic and hydrochloric acids (1 : 1) on a water-bath and yielded coprostenone, m. p. and mixed m. p. 80—81° (Found: C, 84·0; H, 11·2. Calc. for $C_{27}H_{44}O$: C, 84·3; H, 11·5%). Coprostenone was also isolated, and identified by the usual methods, from the reaction products obtained by heating the *trans*-diol with anhydrous copper sulphate to 180° under reduced pressure, or with water in a sealed tube to 200°.

trans-*Cholestene*-3 : 4-*diol from "Oxycholesterol."*—The reaction product obtained according to Lifschütz (*loc. cit.*) from cholesterol (50 g.), brominated in ethereal solution, was poured into water and extracted with light petroleum (1500 c.c.). The extract was filtered through a folded filter, and the extraction repeated until a drop of 90% trichloroacetic acid no longer produced a blue spot on the filter-paper used for filtration. Well-formed orthorhombic crystals were deposited from the extracts on standing. They were collected, and washed with light petroleum; yield 1·5 g., m. p. 235—236°. On recrystallisation from ethyl acetate (1 : 600), the m. p. was raised to 242—244°, but complete purification was only effected by acetylation and subsequent hydrolysis of the diacetate, yielding *trans*-cholestene-3 : 4-diol, m. p. 256—258° (Found: C, 80·5; H, 11·5%). The diacetate, m. p. 135—136°, not depressed in admixture with the diacetate obtained by the selenium dioxide process, crystallised in long needles from methyl alcohol (Found: C, 76·5; H, 10·2%). The results of titrations with perbenzoic acid and with bromine were identical with those given above for the *trans*-diol prepared from cholesteryl acetate and selenium dioxide. On treatment with Brady's reagent, coprostenone-2 : 4-dinitrophenylhydrazone, m. p. 233—234°, was obtained (Found: N, 10·1%).

The diol gives with the Lifschütz reagent (acetic–sulphuric acid, 1 : 10), and also with trichloroacetic acid, the intense blue colour reaction which is considered typical for "oxycholesterol" by Lifschütz. On addition of a drop of dilute ferric chloride, the blue colour changes to green, the second phase of the reaction, showing a well-marked absorption band at 6500 A. characteristic of "oxycholesterol."

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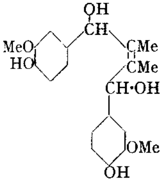
80. *The Constituents of Natural Phenolic Resins. Part VIII. Lariciresinol, Cubebin, and Some Stereochemical Relationships.*

By ROBERT D. HAWORTH and WILLIAM KELLY.

INJURY of the bark of the European larch (*Larix decidua*) leads to the exudation of resin (Überwallungsharz), from which Bamberger (*Monatsh.*, 1897, **18**, 481; 1899, **20**, 647, 745; 1900, **21**, 564; 1902, **23**, 1022; 1903, **24**, 209; 1917, **38**, 457) isolated vanillin, caffeic acid, and the phenolic resinol, lariciresinol. The molecular formula, $C_{19}H_{22}O_6$, was adopted for the resinol, and the presence of two methoxyl, two phenolic, and two alcoholic hydroxyl groups was suggested. Meyer and Jacobson ("Lehrbuch der Organischen Chemie," 1924, II, **4**, 166), however, without producing any additional experimental evidence, suggested $C_{20}H_{24}O_6$, and advanced structure (I) to account for the reactions of the resinol. The orientation of the methoxyl and phenolic groups was inferred from Bamberger's isolation of dinitroguaiacol by the action of nitric acid on lariciresinol, and the formation of guaiacol and pyroguaiacin by distillation of the resinol indicated a relationship with guaiaretic acid (II). In view of the biogenetic relationships of other phenolic resinols,

a C_{20} formula was preferable, and the results of a re-examination of the chemistry of lariciresinol are reported in the present communication.

An improved method of isolation has been developed, and new analyses made on the dextrorotatory resinol and its derivatives support the formula $C_{20}H_{24}O_6$. Zeisel determinations on lariciresinol confirmed the existence of two methoxyl groups, but Zerewitinoff estimations indicated the presence of only three hydroxyl groups. Of these, two are phenolic, and alkali-insoluble *dimethyl* and *diethyl ethers*, m. p. 80° and 104°, respectively, have been prepared by alkylation in alkaline solution. These ethers contained one hydroxyl group only, and as gummy hydrogen phthalates were obtained by the action of phthalic anhydride on the ethers in boiling benzene solution, the hydroxyl group is probably primary alcoholic in character. The ethers were saturated and stable towards alkaline and carbonyl reagents, and were recovered unchanged after treatment with methylmagnesium iodide; the sixth oxygen atom is therefore ethereal in nature.



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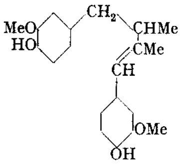

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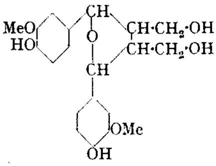
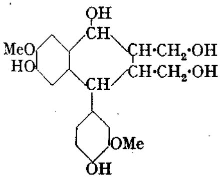


(III.)

Attempts to prepare nitro- or bromo-substitution products of lariciresinol and its ethers were unsuccessful, and this abnormality was traced to the extreme sensitivity of the resinol towards acidic reagents. Lariciresinol was isomerised by boiling with dilute formic acid or with methyl alcohol containing traces of either hydrochloric or acetic acid; the isomer, d-*isolariciresinol*, m. p. 112°, separated with water of crystallisation, and the anhydrous form contained two methoxyl and four hydroxyl groups. The isomerisation therefore involved the conversion of the ethereal oxygen atom of lariciresinol into a hydroxyl group, and this was supported by analyses of d-*isolariciresinol dimethyl* and *diethyl ethers*. The stability of lariciresinol towards water, alkalis, and Grignard reagents was inconsistent with an ethylene oxide structure, and the lariciresinol–*iso*lariciresinol change resembled the conversion of olivil (III) into *iso*olivil (IV) (Vanzetti, *Gazzetta*, 1929, **59**, 373), which is also catalysed by very dilute acids. Potassium permanganate oxidised



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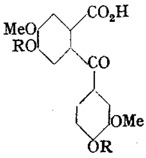

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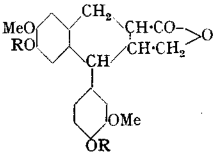
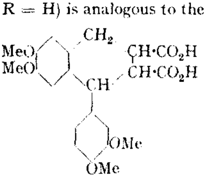


(VI.)

the dimethyl and the diethyl ether of lariciresinol to veratric and 3-methoxy-4-ethoxybenzoic acids respectively; it follows that lariciresinol contains at least one guaiacol group, but the yields of oxidation products were insufficient to establish the presence of two such groups. When *iso*lariciresinol dimethyl ether was oxidised with permanganate, it yielded 2-veratroylveratric acid (V; R = Me) and a similar oxidation of the diethyl ether gave 5-methoxy-4-ethoxy-2-(3′-methoxy-4′-ethoxybenzoyl)benzoic acid (V; R = Et). These observations confirm the view that the conversion of lariciresinol into *iso*lariciresinol involves the cyclisation of a diarylbutane into a 1-phenylnaphthalene derivative, and the

isolation of (V; R = Et) proves that *iso*lariciresinol, and consequently lariciresinol, contain two guaiacol groups. Valuable results have been obtained from a study of the oxidation of *iso*lariciresinol dimethyl ether with sodium hypobromite. *l*-Conidendrin dimethyl ether (" sulphite-liquors lactone " dimethyl ether) (VI; R = Me) was obtained, and identified by comparison with an authentic specimen, and also by dehydrogenation to the lactone of 6 : 7-dimethoxy-1-(3′ : 4′-dimethoxyphenyl)-2-hydroxymethylnaphthalene-3-carboxylic acid (J., 1935, 636). From the acidic oxidation products 2-veratroylveratric acid (V; R = Me) and the dibasic acid (VII) were isolated, and the latter was identified with a specimen prepared by Erdtman (*Annalen*, 1934, **513**, 219) by the action of sodium hypobromite on (VI; R = Me). The formation of (VI; R = Me) and (VII), in which the carbon framework of lariciresinol is retained, indicates formulæ (VIII; R = H) and (IX; R = H), the latter containing a primary alcoholic group, for *iso*lariciresinol and lariciresinol respectively, and the conversion of (IX; R = H) into (VIII; R = H) is analogous to the olivil–*iso*olivil change.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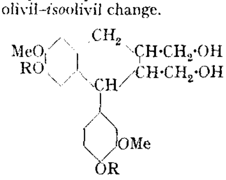
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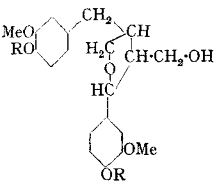
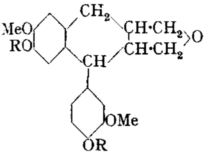

(IX.)

The failure to recognise the facile conversion of lariciresinol (IX; R = H) into *iso*lariciresinol (VIII; R = H) is responsible for several errors in Bamberger's communications (*loc. cit.*). All the compounds described as normal derivatives of lariciresinol (IX; R = H) in his memoirs are derivatives of *iso*lariciresinol (VIII; R = H), and their formation from lariciresinol is due to the influence of acidic reagents. The action of acetyl chloride–pyridine or acetic anhydride–sodium acetate on lariciresinol yielded, in our hands, uncrystallisable products, but lariciresinol was converted by boiling with acetyl chloride into iso*lariciresinol tetra-acetate*, m. p. 162° (previously described as the normal tetra-acetate), giving *iso*lariciresinol (VIII; R = H) on alkaline hydrolysis, and identical with the tetra-acetate obtained by the action of acetic anhydride–sodium acetate on *iso*lariciresinol. Indefinite products were also obtained by the action of non-acidic acetylating agents on the dialkyl ethers of lariciresinol; boiling acetyl chloride, however, converted the ethers into the *diacetates* of the corresponding *iso*-derivatives (previously described as normal diacetates). On alkaline hydrolysis, these diacetates yielded iso*lariciresinol dimethyl* (VIII; R = Me) *and diethyl* (VIII; R = Et) *ethers*, m. p. 167° and 168° respectively (previously described as normal ethers), identical with the ethers obtained by alkylating *iso*lariciresinol. These ethers could not be prepared by alkylation of lariciresinol in alkaline solution as described previously (*Monatsh.*, 1899, **20**, 647, 745), although they were produced if alkylation conditions became acid for a short period. The substance, m. p. 95—97°, prepared by Bamberger (*ibid.*, p. 647) by the action of sodium ethoxide on lariciresinol, is probably impure *iso*lariciresinol, but as lariciresinol is stable to prolonged boiling with sodium ethoxide, the earlier result must be due to the use of excessive acidic conditions during the isolation of the product (see footnote, p. 388). The formation of a diphenolic anhydro-compound (Hermann, *ibid.*, 1902, **23**, 1022) by the action of alcoholic hydrogen chloride on lariciresinol has been confirmed. Alkylation of the anhydro-product, $C_{20}H_{22}O_5$, gave *dialkyl ethers*, and as these were also obtained by heating the dialkyl ethers of either lariciresinol or *iso*lariciresinol with potassium hydrogen sulphate at 180°, it follows that the anhydro-product, $C_{20}H_{22}O_5$, is *anhydro*iso*lariciresinol* (X; R = H). Its *dimethyl ether* (X; R = Me) is saturated and remarkably stable; it was recovered unchanged after treatment with acids, alkalis, sodium in boiling alcohol, acetylating agents, carbonyl reagents, and by sublimation from palladium-black.

During the present research, we were attracted by the possibility that cubebin, the resinol constituent of *Piper cubeba*, might be the methylenedioxy-analogue of lariciresinol. The molecular formula, $C_{20}H_{20}O_6$, containing two methylenedioxy-groups (compare Mameli, *Gazzetta*, 1907, **37**, 483; 1909, **39**, 477, 494; 1912, **42**, 546, 551; 1921, **51**, 353) was consistent with this idea, but the feeble reducing action of lariciresinol dimethyl ether towards Tollens's reagent did not support the analogy. Our thanks are due to Professor G. McOwan of Raffles College, Singapore, for the gift of an alcoholic extract of fresh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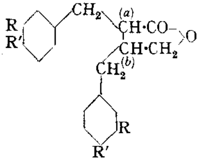
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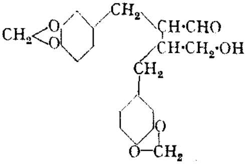
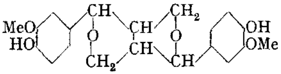
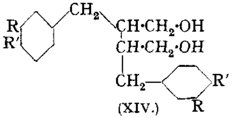

(XII.)

unripe fruit of *Piper cubeba*, from which cubebin was isolated. Analyses confirmed Mameli's formula, Zerewitinoff determinations showed the presence of one hydroxyl group only, but the preparation of a crystalline *semicarbazone* proved that the sixth oxygen atom was aldehydic and not ethereal in function. These results, together with the facile oxidation of cubebin into cubebinolide (XI; RR' = CH_2O_2) (Mameli, *loc. cit.*), established formula (XII), or the corresponding *cyclo*-acetal formula for cubebin, but contemplated confirmatory experiments were abandoned on the appearance of a communication by Ishiguro (*J. Pharm. Soc. Japan*, 1936, **56**, 68) in which similar conclusions were reached.

A comparison of the formulæ of guaiaretic acid (II), matairesinol (XI; R = OMe; R' = OH), olivil (III), lariciresinol (IX; R = H), pinoresinol (XIII; Erdtman, *Annalen*, 1935, **516**, 162), and conidendrin (VI; R = H) reveals an intimate structural relationship


(XIII.)


(XIV.)

which extends also to the methylenedioxy-analogues. Matairesinol (XI; R = OMe; R' = OH) is capable of existing in two resolvable forms, and in the absence of optical inversion, the conversion of *d*-cubebinolide (*l*-hinokinin) (XI; RR' = CH_2O_2; Keimatsu and Ishiguro, *J. Pharm. Soc. Japan*, 1936, **56**, 61) and *l*-arctigenin (Omaki, *ibid.*, 1935, **35**, 9) into *l*-matairesinol dimethyl ether (XI; R = R' = OMe) establishes the common stereochemical configuration of the three compounds. During recent experiments, Ishiguro (*ibid.*, 1936, **56**, 68) reduced cubebin (XII) catalytically to the diol (XIV; RR' = CH_2O_2), which was isolated as an optically active and not as a *meso*-form. From this observation, the significance of which is not indicated in the available abstract (*Centr.*, 1936, ii, 2936), it follows that hinokinin, arctigenin, and matairesinol possess the *trans*-configuration, and it is probable that the synthetic racemates (J., 1936, 725) are the corresponding *cis*-isomers.* The association of *l*-conidendrin and *l*-matairesinol in matai resin, the occurrence of *l*-conidendrin and *d*-pinoresinol in the wood and resin respectively of the spruce, and the conversion of *d*-lariciresinol into *l*-conidendrin described above, suggest that other members of the class may be stereochemically related. By employing

* The terms "*cis*" and "*trans*" refer throughout to the configurations of the centres corresponding to those marked (*a*) and (*b*) in formula (XI), and the arrangement of other asymmetric centres is not considered.

the optically active diol (XIV; R = OMe; R′ = OH) as the hypothetical precursor, and assuming the absence of optical inversion around the centres (*a*) and (*b*) (see footnote, p. 387), it may be deduced that olivil (III) and 1-phenylnaphthalene derivatives, *e.g.*, conidendrin (VI; R = H), possess the *trans*-configuration, and pinoresinol (XIII) and lariciresinol (IX; R = H) represent *cis*-forms. The configurations derived above for olivil and pinoresinol have also been arrived at recently by Erdtman (*Svensk Kem. Tidskr.*, 1936, **48**, 236), without the aid of biogenetic hypotheses, in order to account for the optical activity and the presence of an axis of symmetry in these phenols. Finally, it may be observed that the *cis*-fusion of the two five-membered rings in pinoresinol is consistent with modern views concerning the stability of bicyclic systems, but the configurations for conidendrin and anhydro*iso*lariciresinol (X; R = H) involve a strained *trans*-fusion of five- and six-membered rings.

EXPERIMENTAL.

Lariciresinol (IX; R = H).—The resin was collected from European larches growing in County Durham, particularly from the woods of the Forestry Commission at Chopwell and those belonging to Colonel W. St. A. Warde-Aldam at Healey. Recently felled trees provided the most convenient source of the resin, which exudes from wounds, and was abundant in trees damaged by storm. An old exudate was brittle, transparent, and brown, but a recent flow yielded a viscous, cream-coloured, opaque resin.

The resin (2500 g.), freed as far as possible from bark and wood, was extracted with two lots of boiling alcohol (8 l.), and the extract filtered and concentrated in a vacuum until frothing prevented further removal of solvent. The brown, viscous residue (1500 g., containing approximately 70% of resin) was dissolved in hot alcohol (1 l.), and a solution of potassium hydroxide (900 g.) in water (300 c.c.) was added with stirring. The mixture boiled, darkened in colour, and the potassium salt of lariciresinol, which gradually separated on cooling, was collected after 12 hours, dissolved in water, filtered, and impurities removed with ether. The alkaline liquors were acidified to Congo-red by addition of concentrated hydrochloric acid with stirring, and the excess acid was immediately destroyed by addition of sodium bicarbonate.* The brown gum, which solidified on standing, was collected after 12 hours and washed several times with warm sodium bicarbonate solution, in order to remove most of the coloured impurity. The dried buff-coloured solid (270 g.) was dissolved in warm methyl alcohol (1500 c.c.), filtered through a column of alumina, and the filtrate concentrated to 400 c.c.; after 12 hours, almost pure lariciresinol (170 g.), m. p. 164—166°, was collected. For analysis, the cream-coloured product was crystallised twice from methyl alcohol (carbon); small felted needles, m. p. 167—168°, were obtained (Found: C, 66·6, 66·5; H, 6·8, 6·7; OMe, 17·3, 17·3; OH, 15·1, 14·7, 14·5. Calc. for $C_{20}H_{24}O_6$: C, 66·7; H, 6·7; 2OMe, 17·2; 3OH, 14·1%); in acetone (*c*, 2·232) $[\alpha]_D^{14°} = 19·7°$. Lariciresinol was readily soluble in hot methyl or ethyl alcohol, and the solutions gave a green ferric test. It was sparingly soluble in ether, benzene, chloroform, and ethyl acetate. Unsuccessful attempts were made to reduce the resinol catalytically and by the action of sodium amalgam in alkaline solution. Lariciresinol (0·5 g.), sodium (1 g.), and alcohol (10 c.c.) were boiled for 10 hours. The alcohol was removed, water added, the solution acidified, and excess acid neutralised by addition of sodium bicarbonate. The solid was collected, and crystallised from methyl alcohol; lariciresinol (0·48 g.), m. p. 165—166°, was recovered.

Lariciresinol Dimethyl Ether (IX; R = Me).—Methyl sulphate (0·6 c.c.) was gradually added to a solution of lariciresinol (1 g.) in methyl alcohol (10 c.c.) containing potassium hydroxide (0·3 g.). The mixture was boiled for 0·5 hour on the water-bath, further quantities of methyl sulphate (0·6 c.c.) and potassium hydroxide (0·3 g.) were added, and the boiling continued for another 0·5 hour. The methyl alcohol was removed, water added, and the product, isolated with benzene (A), crystallised from ether in colourless prisms (0·7 g.), m. p. 79—80° (Found: C, 67·7, 68·2; H, 7·2, 7·3; OMe, 31·6; OH, 4·5, 5·1. $C_{22}H_{28}O_6$ requires C, 68·0; H, 7·3; 4OMe, 32·0; 1OH, 4·4%). Kuhn–Roth estimations showed the absence of *C*-methyl groups. In acetone (*c*, 2·051) $[\alpha]_D^{14°} = 22°$. An identical product was obtained by methylating lariciresinol with methyl iodide according to Bamberger's directions. *Lariciresinol dimethyl ether* was readily soluble in the usual organic solvents except light petroleum; it separated from concentrated benzene solution in stout colourless prisms, m. p. 40—45°,

* The addition of bicarbonate was necessary to prevent isomerisation of the gummy lariciresinol in the presence of acids. Attempts to liberate the resinol from alkaline solution with carbon dioxide precipitated a monopotassium salt of lariciresinol.

containing benzene of crystallisation, which is readily lost in a vacuum. It gave a copious white precipitate on the addition of methylmagnesium iodide to its ethereal solution; boiling, followed by decomposition with ammonium chloride, resulted in a quantitative recovery of the unchanged ether, m. p. 79—80°. The ether was not reduced by hydrogen in presence of palladium–carbon or Adams's catalyst. The dimethyl ether (0·4 g.) was boiled with concentrated nitric acid (4 c.c.) for 10 minutes, and water added. The product was extracted with ether, washed with sodium bicarbonate solution, and the ether removed; the residue, crystallised from methyl alcohol, yielded 4 : 5-dinitroveratrole (0·2 g.), m. p. 130°, unchanged by admixture with an authentic specimen. Acidification of the bicarbonate washings precipitated an amorphous acid which has not been identified. Lariciresinol dimethyl ether (0·5 g.), phthalic anhydride (0·2 g.), and benzene (10 c.c.) were refluxed for 2 hours. The cold solution was washed with sodium bicarbonate solution, and the washings were acidified; an amorphous acid, almost insoluble in hot water, was precipitated, but this has not been obtained in a crystalline state.

After the extraction of lariciresinol dimethyl ether with benzene (A, above), the alkaline aqueous layer was acidified; the turbid solution gradually deposited crystals of a *monomethyl ether* of iso*lariciresinol*, which separated from methyl alcohol with solvent of crystallisation, and crystallised from benzene in colourless nodules, m. p. 134—135° (Found : C, 67·6; H, 7·1; OMe, 24·5. $C_{21}H_{26}O_6$ requires C, 67·3; H, 7·0; 3OMe, 24·9%). This ether was converted into *iso*lariciresinol dimethyl ether (VIII; R = Me), m. p. 166°, by the action of methyl sulphate and sodium hydroxide.

Lariciresinol diethyl ether (IX; R = Et), prepared in 70% yields by ethylating lariciresinol with ethyl sulphate or ethyl iodide, crystallised from methyl alcohol in colourless rectangular prisms, m. p. 103—104°, which were insoluble in alkali and gave no ferric test (Found : C, 69·0, H, 7·8; OH, 5·1, 4·9. $C_{24}H_{32}O_6$ requires C, 69·2; H, 7·7; 1OH, 4·1%); boiled with concentrated nitric acid (2 c.c.), it (0·2 g.) yielded 4 : 5-dinitro-*O*-ethylguaiacol (0·09 g.), m. p. 150°, and some unidentified acidic material.

iso*Lariciresinol* (VIII; R = H).—(a) Lariciresinol (1 g.) was boiled with water (16 c.c.) and formic acid (4 c.c.) for 0·5 hour; most of the formic acid was then removed in steam, and *iso*lariciresinol (0·8 g.) separated on cooling.

(b) Lariciresinol (3·5 g.) was boiled with methyl alcohol (35 c.c.) containing two drops of concentrated hydrochloric acid for 0·5 hour. Water was added, most of the alcohol removed, and iso*lariciresinol* (2·8 g.) separated on cooling. It crystallised from aqueous methyl alcohol in colourless, stout prisms, m. p. 112° (with frothing), containing solvent of crystallisation (Found : C, 61·6; H, 6·7%), which was removed by drying over phosphoric oxide in a vacuum at 40—50° for 3 days (Found : C, 66·4; H, 6·8; OMe, 17·1; OH, 19·5. $C_{20}H_{24}O_6$ requires C, 66·7; H, 6·7; 2OMe, 17·2; 4OH, 18·9%). In acetone (*c*, 3·418), $[\alpha]_D^{14°}$ = 69·4°. *iso*Lariciresinol gave a green ferric test; it was not converted into lariciresinol by crystallisation from benzene (compare Bamberger, *Monatsh.*, 1899, **20**, 745).

iso*Lariciresinol tetra-acetate*. (*a*) *iso*Lariciresinol (1 g.) was gently boiled with acetic anhydride (10 c.c.) and sodium acetate (1 g.) for 2 hours, the mixture was diluted with water, and the solid (1·4 g.) collected after 12 hours. (*b*) *iso*Lariciresinol (1 g.) was dissolved in pyridine (10 c.c.), and acetyl chloride (5 g.) gradually added; after 2 hours, the mixture was diluted and the product (1·4 g.) collected. (*c*) Lariciresinol (2 g.) and acetyl chloride (20 c.c.) were gently refluxed for 2 hours. Excess acetyl chloride was removed by distillation, the residue was poured into water, and the solid (2·8 g.) collected after 12 hours. The *tetra-acetate*, obtained by the three methods, crystallised from alcohol in colourless felted needles, m. p. 162° (Found : C, 63·6; H, 5·9; OMe, 11·8; CH_3·CO, 32·6. $C_{28}H_{32}O_{10}$ requires C, 63·6; H, 6·1; 2OMe, 11·8; 4CH_3·CO, 32·6%). In acetone (*c*, 2·285) $[\alpha]_D^{15°}$ = 18·4°. It was insoluble in sodium hydroxide solution and did not give a ferric test. Hydrolysis with methyl-alcoholic potassium hydroxide yielded *iso*lariciresinol, m. p. 112° (with frothing).

iso*Lariciresinol dimethyl ether* (VIII; R = Me), obtained in 95% yields by methylating *iso*lariciresinol with methyl sulphate and sodium hydroxide in the usual way, separated from aqueous methyl alcohol in colourless needles, m. p. 166—167°, containing solvent of crystallisation (Found, after drying at 100° : C, 65·0; H, 7·1; OMe, 30·4, 30·7. $C_{22}H_{28}O_6,H_2O$ requires C, 65·0; H, 7·4; 4OMe, 30·5%. Found, after drying over phosphoric oxide in a vacuum at 100° : C, 67·9; H, 7·4; OMe, 32·0; OH, 9·4. $C_{22}H_{28}O_6$ requires C, 68·0; H, 7·3; 4OMe, 32·0; 2OH, 8·8%). Kuhn–Roth estimations proved the absence of *C*-methyl groups. In chloroform (*c*, 1·950) $[\alpha]_D^{14°}$ = 20°. Unsuccessful attempts were made to reduce the ether catalytically. Lariciresinol dimethyl ether (IX; R = Me) was boiled for 2 hours with acetyl

chloride (10 parts). The product, which was not purified, was hydrolysed with 10% methyl-alcoholic potassium hydroxide; *iso*lariciresinol dimethyl ether (VIII; R = Me), m. p. 166—167°, was obtained.

iso*Lariciresinol diethyl ether* (VIII; R = Et), prepared similarly by ethylating *iso*lariciresinol with ethyl sulphate, separated from alcohol in colourless needles, m. p. 168° (Found: C, 68·8; H, 7·8; OH, 8·9. $C_{24}H_{32}O_6$ requires C, 69·2; H, 7·7; 2OH, 8·2%). The *diacetate*, prepared either (*a*) by boiling *iso*lariciresinol diethyl ether (0·5 g.) with acetic anhydride (5 c.c.) and sodium acetate (0·5 g.) for 2 hours, or (*b*) by boiling lariciresinol diethyl ether (0·5 g.) with acetyl chloride (5 c.c.) for 2 hours, separated from methyl alcohol in felted needles, m. p. 114—115° (Found: C, 66·9; H, 7·1; $CH_3\cdot CO$, 16·8. $C_{28}H_{36}O_8$ requires C, 67·2; H, 7·25; $2CH_3\cdot CO$, 17·2%). In acetone (*c*, 2·869) $[\alpha]_D^{15°}$ = 21·7°. This diacetate was not reduced catalytically, and on hydrolysis with methyl-alcoholic potassium hydroxide it yielded *iso*lariciresinol diethyl ether (VIII; R = Et), m. p. 168°.

*Anhydro*iso*lariciresinol* (X; R = H).—Lariciresinol (2 g.) and saturated methyl-alcoholic hydrogen chloride (7 c.c.) were refluxed for 3 hours; a crystalline compound separated. The mixture was steam-distilled—the distillate had a pronounced odour of guaiacol—and the non-volatile portion deposited an oil, which solidified on cooling. This was collected, and crystallised from methyl alcohol; *anhydro*iso*lariciresinol* (1·3 g.) separated in colourless prisms, m. p. 209—210° (Found: C, 70·0; H, 6·6; OH, 10·8. $C_{20}H_{22}O_5$ requires C, 70·2; H, 6·5; 2OH, 9·9%), which gave a green ferric test. In glacial acetic acid (*c*, 2·157) $[\alpha]_D^{14°}$ = 7·9°. The methyl-alcoholic mother-liquors contained *iso*lariciresinol, m. p. 112° (with frothing), which was isolated by dilution with water.

*Anhydro*iso*lariciresinol dimethyl ether* (X; R = Me), obtained (*a*) by methylating the above phenol (X; R = H) with methyl sulphate and sodium hydroxide or (*b*) by heating the dimethyl ether of either lariciresinol or *iso*lariciresinol with potassium hydrogen sulphate (2 parts) at 180° for 0·5 hour, crystallised from methyl alcohol in jagged prisms, m. p. 146—147° (Found: C, 71·2; H, 6·9. $C_{22}H_{26}O_5$ requires C, 71·4; H, 7·1%). In acetone (*c*, 2·904) $[\alpha]_D^{16°}$ = − 33·4°. Zerewitinoff estimations showed the absence of hydroxyl groups. This ether was heated with palladium-black at 230° for 0·5 hour, and was recovered in 95% yield by subliming at 250°/0·1 mm.

*Anhydro*iso*lariciresinol diethyl ether* (X; R = Et), prepared as for the dimethyl ether (method *b*), crystallised from methyl alcohol in long, rectangular prisms, m. p. 132—133° (Found: C, 72·0; H, 7·5. $C_{24}H_{30}O_5$ requires C, 72·4; H, 7·6%).

Oxidations with Potassium Permanganate.—(*a*) Finely divided permanganate (2 g.) was gradually added during 2 hours to a vigorously stirred suspension of lariciresinol dimethyl ether (IX; R = Me) (0·5 g.) in water (200 c.c.) at 100°. After passage of sulphur dioxide through the cold mixture, the solution was concentrated to 50 c.c., acidified with dilute sulphuric acid, and extracted three times with ether. The extract was washed with sodium bicarbonate solution, the acid recovered, and collected (0·25 g.); recrystallisation from hot water gave veratric acid (0·20 g.), m. p. 180°, unchanged by admixture with an authentic specimen.

(*b*) A similar oxidation of the diethyl ether (IX; R = Et) yielded an acid (0·15 g.), m. p. 194°, unchanged by admixture with 3-methoxy-4-ethoxybenzoic acid.

(*c*) Finely powdered permanganate (7·2 g.) was added during 5 hours to a stirred suspension of *iso*lariciresinol dimethyl ether (VIII; R = Me) (1·5 g.) in water (450 c.c.) at 40—45°. The acidic product (0·1 g.), isolated as described in (*a*) above, separated from aqueous acetic acid in colourless prisms (0·05 g.), m. p. and mixed m. p. with 2-veratroylveratric acid (V; R = Me), 222°. The identity was confirmed by preparing the methyl ester, m. p. 161° (Vanzetti and Dreyfuss, *Gazzetta*, 1934, **64**, 391), and by converting the acid into 2 : 3 : 6 : 7-tetramethoxyanthraquinone, m. p. 344° (Haworth and Mavin, J., 1931, 1365). The neutral oxidation products have not been investigated.

(*d*) Similar oxidation of the *iso*diethyl ether (VIII; R = Et) yielded 5-methoxy-4-ethoxy-2-(3′-methoxy-4′-ethoxybenzoyl)benzoic acid (V; R = Et) (0·06 g.), m. p. 214°, unchanged by admixture with an authentic specimen (Vanzetti and Dreyfuss, *loc. cit.*).

Oxidation of iso*Lariciresinol Dimethyl Ether* (VIII; R = Me) *with Sodium Hypobromite.*—A solution of sodium hypobromite, prepared by the addition of bromine (1·2 c.c.) to 10% sodium hydroxide solution (30 c.c.), was added to a solution of *iso*lariciresinol dimethyl ether (1 g.) in dioxan (8 c.c.). After being heated on the water-bath for 0·5 hour, the solution was boiled for 2 hours, cooled, saturated with sulphur dioxide, acidified with dilute sulphuric acid, and extracted with chloroform. The chloroform solution was extracted several times with sodium

bicarbonate solution (A), and the extract acidified and boiled for 15 minutes. Excess sodium bicarbonate was added, and the mixture digested on the water-bath for 0·5 hour. The solid lactone was collected (B), and crystallised from methyl alcohol; slender needles, m. p. and mixed m. p. with *l*-conidendrin dimethyl ether (VI; R = Me), 174—175° (Found: C, 68·6; H, 6·4. Calc. for $C_{22}H_{24}O_6$: C, 68·7; H, 6·3%). This lactone was dehydrogenated with lead tetra-acetate as described previously (J., 1935, 636); the lactone of 6 : 7-dimethoxy-1-(3′ : 4′-dimethoxyphenyl)-2-hydroxymethylnaphthalene-3-carboxylic acid, m. p. and mixed m. p. 214—215°, was obtained. The bicarbonate liquors (B), from which the conidendrin dimethyl ether had separated, were acidified with acetic acid (C), the solid collected, dried, and esterified by boiling with 10% methyl-alcoholic sulphuric acid (50 parts) for 5 hours. The crude methyl ester, isolated with chloroform, was subjected to fractional crystallisation from methyl alcohol. The sparingly soluble ester separated in long rectangular prisms, m. p. 161° (Found: C, 63·2; H, 5·6. Calc. for $C_{19}H_{20}O_7$: C, 63·3; H, 5·6%), which gave no depression in m. p. with a specimen of methyl 2-veratroylveratrate. Hydrolysis of the ester yielded 2-veratroylveratric acid (V; R = Me), m. p. and mixed m. p. 221—222°. The more soluble ester separated from the mother-liquors; a second crystallisation from methyl alcohol yielded slender needles, m. p. 148—149° (Found: C, 64·8; H, 6·5. Calc. for $C_{24}H_{28}O_8$: C, 64·9; H, 6·4%), which gave no depression in m. p. with methyl 6 : 7-dimethoxy-1-(3′ : 4′-dimethoxyphenyl)-1 : 2 : 3 : 4-tetrahydronaphthalene-2 : 3-dicarboxylate (Erdtman, *loc. cit.*). Hydrolysis yielded the corresponding acid (VII), m. p. and mixed m. p. 192°. Addition of dilute sulphuric acid to the acid liquors (C) precipitated a further quantity of acid, which was esterified; a further yield of methyl 2-veratroylveratrate was obtained. The chloroform solution (A) was evaporated, and the residual oil refluxed with 10% methyl-alcoholic potassium hydroxide for 1 hour; the alcohol was removed, water added, and unchanged *iso*lariciresinol filtered off. Acidification of the filtrate gave a further crop of *l*-conidendrin dimethyl ether (VI; R = Me), m. p. 175°, and an amorphous acid which has not been investigated further.

Cubebin (XII).—The alcoholic extract of *Piper cubeba* was concentrated, and the residual green oil (200 g.) distilled in steam in order to remove the essential oil. The hot residue was made alkaline with sodium hydroxide, cooled, and extracted with ether. The solvent was removed from the dried extract, and the residue crystallised four times from methyl alcohol (carbon); cubebin (2 g.) was obtained as slender prisms, m. p. 132° (Found: C, 67·4, 67·3; H, 5·7, 5·7; OH, 5·2, 5·4. Calc. for $C_{20}H_{20}O_6$: C, 67·4; H, 5·7; 1OH, 4·8%). In acetone (c, 2·757) $[\alpha]_D^{14°} = -17·1°$, changed by a drop of ammonia to $-49·7°$. The *semicarbazone* was prepared by boiling cubebin (0·1 g.) with semicarbazide hydrochloride (0·05 g.) and sodium acetate (0·04 g.) in alcohol (7 c.c.) for 6 hours. Most of the alcohol was removed, water added, and the solid collected and crystallised from methyl alcohol; colourless nodules (0·08 g.), m. p. 144°, were obtained (Found: C, 60·7; H, 5·8; N, 10·3. $C_{21}H_{23}O_6N_3$ requires C, 61·0; H, 5·6; N, 10·2%).

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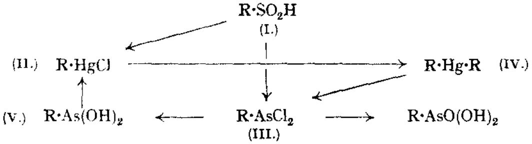
81. *The Preparation of Camphor-10-dichloroarsine from Camphor-10-sulphinic Acid.*

By James D. Loudon.

The formation of organo-mercury compounds from sulphinic acids by the method discovered by Peters (*Ber.*, **1905**, **38**, 2567) suggests the possibility of utilising these acids as a source of organic derivatives of other metals or metalloids which form with carbon a link of sufficient stability to survive the reaction conditions. It has previously been shown (Loudon, J., **1933**, 823) that, with mercuric chloride, camphor-10-sulphinic acid (I) furnishes camphor-10-mercurichloride (II) and it has been found that the corresponding *dichloroarsine* (III) is readily produced by a similar process employing arsenic trichloride. The nature of the product is established by an alternative preparation from arsenic trichloride and biscamphor-10-mercury (IV), and by the interesting observation that it is hydrolysed

to a stable *arsinic acid* (V), from which, by treatment in aqueous solution with mercuric chloride, camphor-10-mercurichloride is quantitatively produced.



R = camphor-10-radical

Although no other instance of this type of arsenuration has, to the author's knowledge, been published, Kharasch (*J. Amer. Chem. Soc.*, 1921, **43**, 610, footnote) also claims to have observed the same reaction in cases which are not specified. The reaction does not, however, appear to be of general application, since with *p*-toluenesulphinic acid and naphthalene-2-sulphinic acid reduction products chiefly resulted.

Experimental.

Camphor-10-dichloroarsine.—(A) A mixture of camphor-10-sulphinic acid (10 g. of oil) and arsenic trichloride (9 g.) was heated for 3—4 hours at 100°. The formation of sulphur dioxide was quickly perceptible. The excess of arsenic trichloride together with some water (which always appeared and was probably introduced with the sulphinic acid) were distilled off under reduced pressure and the residue, which solidified on cooling, was extracted with ether (charcoal). Concentration of the extract yielded a crystalline mass which, after repeated crystallisation from light petroleum, was obtained in long colourless needles, m.p. 89—90°.

(B) Biscamphor-10-mercury (5 g.) and arsenic trichloride (20 g.) were refluxed on an oil-bath (190—200°) for 3—4 hours and the product was worked up as in (A). To separate the *dichloroarsine* from camphor-10-mercurichloride, the ethereal extract after evaporation was again extracted with small quantities of hot petroleum, from which the dichloroarsine separated on cooling; m. p. and mixed m. p. 89—90° (Found: C, 40·2; H, 5·05; Cl, 23·6. $C_{10}H_{15}OCl_2As$ requires C, 40·4; H, 5·05; Cl, 23·9%).

Camphor-10-arsinic Acid.—Camphor-10-dichloroarsine was shaken with warm concentrated sodium hydroxide solution until complete dissolution was effected. The precipitate obtained by acidification (after cooling) was recrystallised from hot water and formed long needles, m. p. 100° (decomp.) (Found: C, 43·4; H, 6·8. $C_{10}H_{17}O_3As,H_2O$ requires C, 43·2; H, 6·8%). When a suspension of the *compound* in benzene or light petroleum was gently warmed, it appeared first partly to dissolve and then suddenly to lose water. A white insoluble powder, melting indefinitely at 190°, was produced, but could not be purified and had a somewhat variable composition (Found: C, 33·9, 34·2; H, 4·9, 5·7%).

Camphor-10-mercurichloride was formed in excellent yield when an aqueous solution of the arsinic acid (0·5 g.) and mercuric chloride (0·5 g.) was heated for 1 hour. The solid formed was extracted with chloroform, and the extract recrystallised from alcohol; m. p. and mixed m. p. with an authentic specimen, 166—167°.

Camphor-10-arsonic acid was obtained by concentrating the solutions produced (1) by passing chlorine into an aqueous suspension of the dichloroarsine and (2) by oxidising the same compound with hydrogen peroxide in acetic acid. The product crystallised from alcohol in massive prisms or in fine needles, melting in each case at 210° (Found: C, 43·2; H, 6·3. $C_{10}H_{17}O_4As$ requires C, 43·5; H, 6·2%). The barium salt was more soluble in cold than in hot water.

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82. *Polycyclic Aromatic Hydrocarbons. Part XV. New Homologues of* 1 : 2-*Benzanthracene.*

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The unsymmetrical 1 : 2-benzanthracene molecule contains no less than 12 positions of monosubstitution (see formula VI), and as this molecule is endowed with latent carcinogenic activity, a systematic study of benzanthracene derivatives has been in progress here for some years in order to define the nature and positions of substituents necessary for the development of cancer-producing properties. Seven of the 12 possible monomethylbenzanthracenes have been described (Cook, J., 1930, 1087; 1932, 456; 1933, 1592). Three more have since been prepared, and their synthesis is now recorded on account of the preparation by Fieser and Newman (*J. Amer. Chem. Soc.*, 1936, **58**, 2376) of one of our new homologues (10-methyl-1 : 2-benzanthracene) by a different method. The two methylbenzanthracenes which now remain unknown are the 8- and the 1′-compound, and we are engaged in their synthesis.

Of the 7 methylbenzanthracenes which have had adequate biological test, the 5-methyl compound gave malignant tumours in a large proportion of the mice, although the appearance was considerably delayed; the 6-methyl compound had very feeble activity; the 4-methyl compound gave one non-malignant tumour, and the other compounds were inactive (Barry, Cook, Haslewood, Hewett, Hieger, and Kennaway, *Proc. Roy. Soc.*, 1935, *B*, **117**, 318). These results, coupled with the fact that nearly all of the highly active carcinogenic compounds have additional rings attached at position 5 of the benzanthracene ring system, suggested that substitution at this position is especially favourable for carcinogenic activity. This is further borne out by the fact that both 5-*ethyl*-1 : 2-*benzanthracene* (now described) and 5-*n*-propyl-1 : 2-benzanthracene (Cook and Haslewood, J., 1935, 767) are moderately potent carcinogenic compounds. For these biological tests we are indebted to Professor E. L. Kennaway.

Commenting on the carcinogenic potency of cholanthrene and methylcholanthrene, Fieser and Newman (*loc. cit.*) remark "that it is a matter of considerable interest to attempt to define the features of structure responsible for their striking activity," a sentiment with which we are in complete agreement. Then, on the basis of the carcinogenic activity of their newly-synthesised 5 : 10-dimethyl-1 : 2-benzanthracene and of ulcerations obtained in mice after injection of 10-methyl-1 : 2-benzanthracene during a period in which 5-methyl-1 : 2-benzanthracene was without effect, these authors infer that "the five-membered ring characteristic of the cholanthrene system is of importance in contributing to the carcinogenic potency of hydrocarbons of this type only in that it includes carbon substituents at the 5- and 10-positions. The presence of the intact ring is by no means essential, for simple alkyl groups at these positions produce nearly the same effect. Substitution at the meso-position 10 seems to be particularly important." * We regard this last conclusion as premature. The only 10-alkylbenzanthracene which has received adequate biological test is the 10-*iso*propyl compound, which gave completely negative results in an experiment lasting 611 days (Barry *et al.*, *loc. cit.*). Tests with our sample of 10-methyl-1 : 2-benzanthracene have been in progress for only 130 days, so that we are not in a position to comment on its activity or otherwise, except to say that no tumours have yet arisen.

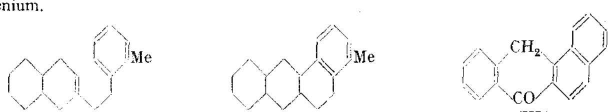
From the facts at present available, the conclusion seems warranted that position 5 is the most favourable position of substitution for carcinogenic activity in derivatives of 1 : 2-benzanthracene, and that the influence of the group in this position may be re-

* This theme has been further elaborated by Fieser in two papers which have appeared since the present communication was submitted for publication (Fieser and Hershberg, *J. Amer. Chem. Soc.*, 1937, **59**, 394; L. F. Fieser, M. Fieser, Hershberg, Newman, Seligman, and Shear, *Amer. J. Cancer*, 1937, **29**, 260). It is stated in these papers that 10-methyl-1 : 2-benzanthracene has high cancer-producing activity comparable with that of the cholanthrene group. We prefer to defer discussion of this question until the biological testing of our own specimen of 10-methyl-1 : 2-benzanthracene is complete.

inforced by a second substituent at position 6 or 10 (compare Cook, *Bull. Soc. chim.*, in the press).

For the synthesis of 5-ethyl-1 : 2-benzanthracene, 5-ketododecahydro-1 : 2-benzanthracene was treated with ethylmagnesium bromide, and the crude tertiary carbinol dehydrated and dehydrogenated. This highly hydrogenated ketone seemed more suitable than the sparingly soluble 5-ketotetrahydro-1 : 2-benzanthracene used for the preparation of 5-methyl-1 : 2-benzanthracene (*J.*, 1933, 1592). Extension to the synthesis of higher 5-alkylbenzanthracenes has been impeded by the variable compositions of different batches of *as*-octahydrophenanthrene used in the preparation of ketododecahydrobenzanthracene (Cook and Haslewood, *loc. cit.*), which led to the isolation, from some batches, not of the desired tetracyclic ketone, but of an isomeric ketone derived from 1-hydrindene*spirocyclo*hexane present in the "octahydrophenanthrene." These experiments form part of a separate study of the stereochemistry of hydrophenanthrene derivatives, and will be reported later.

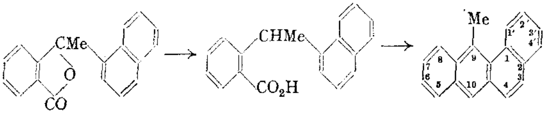
4'-Methyl-1 : 2-benzanthracene was synthesised by extension of the benzanthracene synthesis of Cook and Hewett (*J.*, 1934, 365), for which purpose 2-(β-o-*tolylethyl*)-trans-2-*decalol* was dehydrated to the corresponding *octalin* (I), which was cyclised to *4'-methyl-dodecahydro-1 : 2-benzanthracene* (II), the latter being finally dehydrogenated with selenium.



(I.) (II.) (III.)

10-Methyl-1 : 2-benzanthracene was obtained by the action of methylmagnesium iodide on 1 : 2-benz-10-anthrone (III). The m. p.'s of the hydrocarbon and its picrate agreed with those recorded by Fieser and Newman (*loc. cit.*), who used a completely different method of synthesis.

An attempt to obtain 9-methyl-1 : 2-benzanthracene by a similar Grignard condensation with 1 : 2-benz-9-anthrone was unsuccessful, and this hydrocarbon was thereupon prepared by a method which is essentially that employed by Fieser and Newman for the 10-methyl compound, although our own experiments were completed before the appearance of their paper. 1-Naphthoylbenzoic acid reacted smoothly with an excess of methylmagnesium iodide to give (1-*naphthyl*)*methylphthalide* (IV) which, after hydrolysis with alcoholic alkali, was reduced by zinc dust and sodium hydroxide to o-α-(1-*naphthyl*)-*ethylbenzoic acid* (V). This was dehydrated by zinc chloride to the corresponding anthrone, which was immediately reduced with zinc dust and alkali, giving *9-methyl-1 : 2-benzanthracene* (VI) in good yield.



(IV.) (V.) (VI.)

Experimental.

5-Ethyl-1 : 2-benzanthracene.—5-Ketododecahydro-1 : 2-benzanthracene (Cook and Haslewood, *loc. cit.*) (3 g.) was added to an ice-cold Grignard reagent from ethyl bromide (1·33 g.) and magnesium turnings (0·3 g.) in anhydrous ether (20 c.c.). The whole was then heated on the water-bath for 2 hours, decomposed with ice and ammonium chloride, and the ether removed from the dried extract. The crude carbinol was dehydrated with potassium hydrogen sulphate at 160°, and the distilled hydrocarbon (b. p. 161—165°/0·2 mm.; 3 g.) was dehydrogenated with platinum-black at 300°. The product was treated with picric acid in benzene, and the

dark red picrate was recrystallised from benzene until it had constant m. p. 150—151° (yield 1·1 g.). The regenerated *5-ethyl-1 : 2-benzanthracene* crystallised from alcohol in colourless leaflets, m. p. 120° (Found : C, 93·2; H, 6·3. $C_{20}H_{16}$ requires C, 93·7; H, 6·3%).

5-Ethyl-1 : 2-benzanthraquinone, obtained by boiling a solution of the hydrocarbon (0·1 g.) and sodium dichromate (0·2 g.) in acetic acid (3 c.c.) for 10 minutes, crystallised from methyl alcohol in orange needles, m. p. 97—98° (Found : C, 83·65; H, 5·0. $C_{20}H_{14}O_2$ requires C, 83·9; H, 4·9%).

9-Methyl-1 : 2-benzanthracene.—Finely powdered *o*-1-naphthoylbenzoic acid (18·7 g.) was added gradually to an ice-cold Grignard solution prepared from methyl iodide (20 g.), magnesium turnings (3·3 g.), and anhydrous ether (150 c.c.). The flask was shaken vigorously in order to powder the precipitated magnesium complex. The suspension was boiled for 2 hours, and then decomposed with dilute sulphuric acid. The ethereal layer deposited crystals of (1-*naphthyl*)*methylphthalide* (IV) (7·5 g.), which, after washing with dilute sodium carbonate, were recrystallised from alcohol and then light petroleum, forming thick colourless plates, m. p. 152—153° (Found : C, 83·3; H, 5·4. $C_{19}H_{14}O_2$ requires C, 83·2; H, 5·1%).

This phthalide (18 g.) was hydrolysed with sodium hydroxide (18 g.) in boiling alcohol (300 c.c.), and the alcohol distilled off. Then water (300 c.c.) and concentrated ammonium hydroxide (75 c.c.) were added, and the solution boiled with zinc dust (35 g.) for 24 hours. The filtered solution was acidified, and the precipitated o-α-(1-*naphthyl*)*ethylbenzoic acid* (V) was recrystallised from aqueous alcohol, forming colourless needles (15·5 g.), m. p. 167—168° (Found : C, 82·7; H, 6·05. $C_{19}H_{16}O_2$ requires C, 82·6; H, 5·8%).

Cyclisation of this acid (10 g.) was effected by heating with anhydrous zinc chloride (30 g.) at 180° for 20 minutes. After cooling, the mass was powdered, and extracted with dilute hydrochloric acid, and then dilute sodium carbonate solution. The crude residual anthrone was then suspended in 2*N*-sodium hydroxide solution (300 c.c.) and boiled with zinc dust (20 g.) for 3 hours. The solid was collected, excess zinc extracted with hydrochloric acid, and the hydrocarbon recrystallised from acetic acid. The *9-methyl-1 : 2-benzanthracene* (VI) (5·2 g.), m. p. 136—139°, was purified through its *picrate*, which crystallised from benzene in dark red needles, m. p. 115—116° (Found : C, 63·7; H, 4·5.* $C_{25}H_{17}O_7N_3$ requires C, 63·7; H, 3·6%). The hydrocarbon regenerated from the picrate was sublimed in a vacuum and recrystallised from alcohol, forming yellowish plates, m. p. 138—139° (Found : C, 94·2; H, 6·1. $C_{19}H_{14}$ requires C, 94·2; H, 5·8%). In conformity with its structure (VI), oxidation of this hydrocarbon with sodium dichromate in boiling acetic acid gave 1 : 2-benzanthraquinone, m. p. 168—169°, alone or mixed with an authentic specimen.

10-Methyl-1 : 2-benzanthracene.—Crude 1 : 2-benz-10-anthrone, prepared by zinc chloride dehydration of 1-naphthylphenylmethane-2′-carboxylic acid (Cook, J., 1930, 1093) (20 g.), was added to an ice-cold Grignard solution prepared from methyl iodide (73 g.), magnesium turnings (12 g.), and anhydrous ether (200 c.c.). After an hour at 0°, the whole was heated on the water-bath for 1½ hours. The product was decomposed with ice and ammonium chloride, the ethereal solution dried (sodium sulphate), and the ether removed. The residue (12 g.) was treated, in acetic acid solution, with an equal weight of picric acid. This treatment suffices to complete the dehydration to the hydrocarbon of the primarily formed tertiary carbinol. The dark red crystals were freed from picric acid by extraction with dilute sodium carbonate, and the product extracted with about 20 c.c. of boiling benzene, and filtered. Some dianthrone-like material, m. p. above 300°, evidently the product of atmospheric oxidation of the anthrone, remained undissolved. The hydrocarbon recovered from the filtrate was sublimed at 150°/0·15 mm., and recrystallised from alcohol, forming slender yellowish needles (1·4 g.), m. p. 138°. Final purification was accomplished through the picrate, which crystallised from benzene in dark red needles, m. p. 172—173·5° (corr.) (Found : C, 63·7; H, 3·5. Calc. for $C_{25}H_{17}O_7N_3$: C, 63·7; H, 3·6%). Fieser and Newman (*loc. cit.*) give m. p. 173·5—174° (corr.). 10-Methyl-1 : 2-benzanthracene, regenerated from this picrate, had m. p. 140·5—141·5° (corr.) (Found : C, 94·0; H, 5·85. Calc. for $C_{19}H_{14}$: C, 94·2; H, 5·8%). Fieser and Newman give m. p. 140·2—140·8° (corr.). Oxidation with sodium dichromate in boiling acetic acid gave 1 : 2-benzanthraquinone.

4′-Methyl-1 : 2-benzanthracene.—Thionyl chloride (23 c.c.) was added dropwise with agitation to an ice-cold mixture of β-*o*-tolylethyl alcohol (40 g.) and dimethylaniline (36 g.). The mixture was then heated on the water-bath for ½ hour, and the resulting β-o-*tolylethyl chloride* (40 g.) isolated in the normal way. It formed a colourless liquid, b. p. 100°/15—20 mm. (Found : C, 69·5; H, 7·1. $C_9H_{11}Cl$ requires C, 69·9; H, 7·2%). *trans*-β-Decalone (39 g.) was added to

* The high value for hydrogen is due to unreduced oxides of nitrogen.

an ice-cold Grignard solution prepared from this chloride (40 g.) and magnesium turnings (6·2 g.) in anhydrous ether (200 c.c.). After being kept at room temperature for an hour, the whole was heated on the water-bath for 1½ hours, decomposed with ice and ammonium chloride, and the tertiary carbinol isolated by distillation. 2-(β-o-*Tolylethyl*)-trans-2-*decalol* (40 g.) formed a colourless viscous liquid, b. p. 170—180°/0·6 mm., which slowly crystallised when kept in the ice chest, but could not be satisfactorily recrystallised (Found: C, 83·5; H, 10·5. $C_{19}H_{28}O$ requires C, 83·7; H, 10·4%).

2-(β-o-*Tolylethyl*)-$\Delta^{2:3}$-*octalin* (I) was obtained when this carbinol (37 g.) was heated with potassium hydrogen sulphate (78 g.) at 170—180° for 2 hours. After redistillation over sodium, the octalin formed a colourless liquid (30 g.), b. p. 160—162°/0·7 mm. (Found: C, 89·2; H, 10·2. $C_{19}H_{26}$ requires C, 89·7; H, 10·3%).

For cyclisation, an ice-cold solution of this unsaturated hydrocarbon (I; 28 g.) in carbon disulphide (280 c.c.) was treated gradually with anhydrous aluminium chloride (40 g.), and then kept overnight at room temperature. The clear solution was decanted from the aluminium chloride sludge, washed with dilute acid and dilute alkali, dried, and distilled. Two fractions were collected at 0·2 mm.: (i) b. p. 156—170° (14 g.); (ii) b. p. 170—180° (5 g.). Fraction (ii) crystallised on standing, and was twice recrystallised from methyl alcohol. This crystalline 4'-*methyldodecahydro*-1 : 2-*benzanthracene* (II) formed colourless rectangular plates, m. p. 92·5—93·5° (Found: C, 89·7; H, 10·3. $C_{19}H_{26}$ requires C, 89·7; H, 10·3%). A further quantity of this crystalline isomeride was isolated from fraction (i) by seeding. In all, about 2 g. of the pure material were isolated. Dehydrogenation with selenium at 300° for 24 hours gave in good yield 4'-*methyl*-1 : 2-*benzanthracene*, which was freed from the last traces of selenium by adsorption on alumina, then sublimed at 160—170°/0·2 mm., and the sublimate treated in benzene solution with an equal weight of picric acid. The picrate separated in light red needles, m. p. 139—140°, but was too readily dissociated to be recrystallised. The regenerated hydrocarbon crystallised from benzene in colourless irregular plates, m. p. 194—195° (Found: C, 94·0; H, 5·9. $C_{19}H_{14}$ requires C, 94·2; H, 5·8%). The non-crystalline isomerides of (II) also gave this 4'-methyl-1 : 2-benzanthracene on selenium dehydrogenation.

4'-*Methyl*-1 : 2-*benzanthraquinone*, obtained by oxidation of the foregoing hydrocarbon with sodium dichromate in boiling acetic acid, crystallised from benzene in golden-orange needles, m. p. 219—220° (Found: C, 83·45; H, 4·4. $C_{19}H_{12}O_2$ requires C, 83·8; H, 4·4%).

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83. *The Alkaloids of Ergot. Part VIII. New Alkaloids of Ergot: Ergosine and Ergosinine.*

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To the list of those alkaloids of ergot regarded as definite and well-characterised substances which was given in Part VII (J., 1936, 1440) must now be added two new alkaloids, *ergosine* and *ergosinine*, the isolation of which we have briefly reported elsewhere (*Nature*, 1936, **137**, III, 1075).

Ergosinine probably owes its escape from earlier recognition to the resemblance which it bears to ergotinine and ψ-ergotinine. Like these alkaloids, it is sparingly soluble in methyl alcohol and the specific rotations of ergotinine and ergosinine are almost identical in acetone solution, though they differ in chloroform solution. In the case of ergosinine and ψ-ergotinine the specific rotations are similar in chloroform solution, but differ in acetone solution:

$[\alpha]_{5461}^{20°}$.	Ergotinine.	Ergosinine.	ψ-Ergotinine.
In acetone	+ 478°	+ 475°	+ 509°
In chloroform	+ 464°	+ 522°	+ 512°

Ergosinine is readily isolated by boiling the total water-insoluble alkaloids of ergot with benzene and extracting the benzene-soluble portion with dilute sodium hydroxide

solution. The alkaline extract contains the alkaloids ergotoxine and ergosine and on acidification with sulphuric acid gives a precipitate of ergotoxine sulphate, ergosinine sulphate remaining mainly in solution, a separation which, though not sharp, is adequate for preparative purposes. The solution of the water-soluble sulphates on basification gives a precipitate, from which ergosinine is readily separated by treatment with methyl alcohol. The nearly pure ergosinine so obtained is easily purified by recrystallisation.

Like the other ergot alkaloids of high dextrorotation, ergosinine is partly and easily transformed into a corresponding lævorotatory alkaloid by treatment with acid or alkali. The new alkaloid, ergosine, obtained in this way has $[\alpha]_{5461}^{20^\circ}$ − 193° in chloroform solution and crystallises readily. It is easily reconverted by similar means into ergosinine and the two alkaloids thus constitute a pair with a relationship to each other similar to that existing between the earlier known pairs of ergot alkaloids. The close similarity, in this respect, to the amides and substituted amides of the isomeric lysergic acids (see Parts VI and VII) makes it highly probable that ergosine differs from ergosinine only in the configuration of the lysergic acid portion of the molecule. Ergosinine and ergosine give the colour reactions typical of the ergot alkaloids. With dimethylaminobenzaldehyde the blue colour given by both alkaloids is approximately equal in intensity and slightly greater than that given by ergotinine. This suggests that the two alkaloids are isomeric and that the molecular weight is slightly less than that of ergotinine. Like the other ergot alkaloids, solutions of ergosine and ergosinine fluoresce strongly in daylight and on exposure to ultra-violet light the fluorescence is intense. The absorption spectra of the two alkaloids are similar to those of the other ergot alkaloids. In addition to the characteristic peak at A. 3180 they show the inflexion at A. 2420 which we previously observed in the case of ergotinine (J., 1931, 1889). Ergosinine gives a stronger inflexion than ergosine and in this resembles ergotinine rather than ergotoxine.

In a preliminary announcement (*Nature*, *loc. cit.*) the formula $C_{30}H_{35}O_5N_5$ was tentatively suggested as the result of analyses of the crystalline bases, but the results of degradative experiments (*vide infra*) indicate clearly that the formula $C_{30}H_{37}O_5N_5$ containing two more atoms of hydrogen is correct. Ergosinine has given no crystalline salts, but an amorphous hydrochloride has been obtained. Ergosine forms salts which crystallise with one molecular proportion of acetone. Ergosinine contains no methoxyl group, but one methylimino-group is present, which must be derived from the ergine nucleus (*vide infra*), which is known to contain this group. The ergine group is also probably responsible for the evolution of ammonia which occurs on alkaline hydrolysis, a process which converts ergine into lysergic acid and ammonia. Ergine, $C_{16}H_{17}ON_3$, which has previously been shown to be a nucleus common to the ergot alkaloids (J., 1932, 763, 1543), has also been obtained from ergosinine by alkaline hydrolysis. The latter has also been degraded to lysergic acid, $C_{16}H_{16}O_2N_2$ (Jacobs and Craig, *J. Biol. Chem.*, 1934, **104**, 547; Smith and Timmis, J., 1934, 674), of which ergine is the amide. Alkaline hydrolysis also liberates pyruvic acid, the presence of which in the ergotamine molecule has been reported by Jacobs and Craig (*Science*, 1935, **81**, 256). Another degradation product, leucine, has been obtained from ergosinine by the process of acid hydrolysis first used by Jacobs and Craig (*J. Biol. Chem.*, 1935, **110**, 521) for the cleavage of ergotinine. The only ergot alkaloid which has hitherto given leucine on hydrolysis is ergoclavine (Jacobs and Craig, *J. Amer. Chem. Soc.*, 1935, **57**, 960). The properties of ergoclavine described by Küssner (*Jahresber.*, 1933, **47**, 5; *Arch. Pharm.*, 1934, **272**, 503) are widely different from those of ergosine and ergosinine and according to E.P. specification 7972/1935 it is a mixture of unidentified alkaloids. We have observed that ergosinine and ergosine readily crystallise together from chloroform or ethyl acetate as a molecular *compound*, which is less soluble than either of its components. The pure compound from ethyl acetate melts with decomposition at about 200°, and has $[\alpha]_D^{20^\circ}$ + 128° in chloroform solution. An equimolecular mixture of the two alkaloids would have (by calculation) $[\alpha]_D^{20^\circ}$ + 129°, which is close to the value + 124° given by Küssner (*loc. cit.*) for ergoclavine. The latter, however, melts at 177° and the reported elementary composition differs significantly from that of ergosine and ergosinine. When ergosinine is heated under reduced pressure, it gives rise to several crystalline products, of which the least volatile after purification melts at 148° and according to the

analyses and molecular weight determination must have the formula $C_{11}H_{18}O_2N_2$. On acid hydrolysis it yields only two products, *l*-leucine and *d*-proline, the latter being identified by formation of the aurichloride of the betaine. The substance must therefore be l-*leucyl*-d-*proline lactam* (3 : 6-*diketo*-5-iso*butyl*-1-2-*trimethylenepiperazine*).

In the course of purifying the lactam two other crystalline substances were obtained in quantities too small for complete identification, but neither of these is the amide of pyruvic acid. A crystalline sublimate, highly volatile under reduced pressure, was also produced from ergosinine, but in a very small yield. This proved to be a mixture, but it possibly contained pyruvamide, because it sublimed and melted similarly to this substance and gave evidence of hydrolysis to pyruvic acid and ammonia when it was treated with alkali. The degradation products derived from ergosinine are therefore ergine (or lysergic acid), leucine, proline, and pyruvic acid. The condensation of these four substances with elimination of three molecules of water requires the formula $C_{30}H_{37}O_5N_5$ as suggested above.

Ergosinine has the high specific dextrorotation typical of the physiologically weak ergot alkaloids, whereas ergosine has a specific rotation comparable with that of the physiologically active ergot alkaloids. The pharmacological action of ergosine and ergosinine is at present under investigation by Dr. White (at the Wellcome Physiological Research Laboratories) and the results will be published elsewhere. Briefly, he reports that examination of the actions of ergosine and ergosinine so far shows that they form a pair of alkaloids which show differences analogous to those found with other similar ergot alkaloid pairs, *e.g.*, ergotoxine and ergotinine, and ergotamine and ergotaminine. Ergosine is the more active and in its toxic symptoms closely resembles ergotoxine and ergotamine. The action of ergosine in paralysing the adrenaline response of the rabbit uterus is more powerful than that of ergotoxine.

EXPERIMENTAL.

Isolation of Ergosinine.—The total alkaloids of ergot were extracted with boiling benzene. The solution, after being cooled, was separated from sparingly soluble substances and extracted with 1% sodium hydroxide solution. The extract was made just acid to Congo-red by the addition of dilute sulphuric acid. The precipitate of sparingly soluble sulphates was removed by filtration, and the filtrate basified with sodium bicarbonate. The precipitate so formed, after being dried over sulphuric acid in a vacuum desiccator, was treated with a little methyl alcohol. The resulting crystalline precipitate of crude ergosinine was purified by recrystallisation from hot aqueous acetone. A further quantity was obtained by extracting the precipitate of sparingly soluble sulphates with water, basifying the solution with sodium bicarbonate, and treating the resulting precipitate with methyl alcohol as above.

Ergosinine is very readily soluble in chloroform, readily soluble in acetone, less soluble in ethyl acetate, sparingly soluble in benzene, very sparingly soluble in methyl alcohol, and almost insoluble in water. It crystallises very readily. From 90% alcohol, aqueous acetone, benzene, and ethyl acetate it separates in solvent-free prisms which decompose with blackening and frothing at 228°. From methyl alcohol it separates in needles, m. p. 220° (decomp.), which contain methyl alcohol (Found in air-dried material: MeO, 2·9; loss at 100°, 3·0. $C_{30}H_{37}O_5N_5,\frac{1}{2}MeOH$ requires MeO, 2·8; MeOH, 2·9%). The specific rotations are: $[\alpha]_{5461}^{20°}$ + 522° and $[\alpha]_D^{20°}$ + 420° (in chloroform, $c = 1$), $[\alpha]_{5461}^{20°}$ + 475° and $[\alpha]_D^{20°}$ + 380° (in acetone, $c = 1$); c refers to the solvent-free substance in each case (Found in material crystallised from aqueous acetone: C, 65·8; H, 6·6; N, 12·8; NMe, 6·6; in material crystallised from benzene: C, 65·9; H, 6·6; N, 12·7; in material crystallised from ethyl acetate: C, 66·0; H, 6·7; N, 13·1. $C_{30}H_{37}O_5N_5$ requires C, 65·8; H, 6·8; N, 12·8; NMe, 5·3%). Ergosinine in dilute solution acidified with hydrochloric acid gives precipitates with potassium mercuric iodide, potassium bismuth iodide and mercuric acid sulphate. It gives a blue colour with the dimethylaminobenzaldehyde reagent as modified by Allport and Cocking (*Quart. J. Pharm.*, 1932, **5**, 341) and compared with ergotinine the relative intensities are 102 : 100 and approximately inversely proportional to the molecular weights. Ergosinine gives the other colour reactions typical of the ergot alkaloids: a blue colour with glyoxylic acid, a yellow colour with dilute nitric acid and a trace of sodium nitrite, and in acetic acid a blue colour with sulphuric acid and a trace of ferric chloride.

The absorption spectrum of ergosinine measured between A. 2500 and A. 3500 shows the maximum at A. 3180 and the minimum at A. 2700 typical of the ergot alkaloids. It also shows the less well-defined inflection at A. 2420 which we have recorded in the case of ergotinine and

ψ-ergotinine (J., 1931, 1889). The measurements were made with $M/10,000$ and $M/30,000$ solutions in absolute alcohol.

Ergosinine Hydrochloride.—The base, dissolved in acetone, was treated with excess of 10% hydrochloric acid. The precipitate which first formed soon redissolved and the solution was poured into ether. The salt is amorphous, and readily soluble in water, giving an acid solution from which the *hydrochloride* is precipitated by the addition of hydrochloric acid. It darkens at 200° and decomposes at about 206° (Found: C, 61·8; H, 6·6; N, 12·0; HCl, 6·2. $C_{30}H_{37}O_5N_5$,HCl requires C, 61·8; H, 6·5; N, 12·0; HCl, 6·3%).

The salt prepared by adding 10% sulphuric acid to a solution of the base in acetone and pouring the solution into ether is amorphous, begins to darken at 190°, and decomposes at about 200°. It is a mixture of the normal and the acid sulphate. The nitrate, prepared by precipitating a solution of the base in dilute lactic acid with dilute nitric acid, is also amorphous; it begins to go grey at 190° and decomposes at about 200°.

Alkaline Hydrolysis of Ergosinine.—The base (1 g.) was heated with aqueous potassium hydroxide (8%, 25 c.c.) on a water-bath for 1 hour. The solution, which had a strong odour of ammonia, was acidified (litmus) with acetic acid. The granular precipitate was rapidly crystallised from hot water. Yield, 0·2 g. It darkened at 200°, decomposed at 235°, and had $[\alpha]_{5461}^{20°}$ + 55° (in pyridine, c = 0·4) (Found: C, 71·8; H, 6·2; N, 10·4; NMe, 9·0. Calc. for lysergic acid, $C_{16}H_{16}O_2N_2$: C, 71·6; H, 6·0; N, 10·4; NMe, 10·8%). When treated with alcoholic potassium hydroxide and worked up as described in Part III (J., 1932, 763), ergosinine gave the characteristic needles of ergine, which frothed at 135°.

A portion of the filtrate from the lysergic acid, treated with sodium nitroprusside and potassium hydroxide, gave the red colour, changing to blue on addition of solid ammonium chloride, which is typical of pyruvic acid. The bulk of the filtrate was extracted with ether, the ethereal extract evaporated, and the residue, which had an odour of pyruvic acid, heated with water. The aqueous solution was separated from a little sticky material and treated with phenylhydrazine, potassium acetate and acetic acid. The resulting precipitate crystallised readily from methyl alcohol in needles, m. p. 188°, which did not depress the m. p. of pyruvic acid phenylhydrazone.

Acid Hydrolysis of Ergosinine.—The base (1 g.) was dissolved in concentrated hydrochloric acid (15 c.c.) and heated on a steam-bath for 16 hours. The black solution was diluted with water and extracted with ether. The ethereal extract gave a slight residue on evaporation, but nothing was isolated from it. The aqueous solution was evaporated to dryness. The residue was extracted with water, the solution treated with charcoal and filtered, and the hydrochloric acid removed with silver sulphate. The silver was removed with hydrogen sulphide, and the sulphuric acid with barium carbonate. The filtrate on concentration gave 0·12 g. of irregular plates, which after crystallisation from hot water formed the plates characteristic of leucine (Found: C, 54·8; H, 9·8; N, 10·5. Calc. for $C_6H_{13}O_2N$: C, 55·0; H, 10·0; N, 10·7%). It had $[\alpha]_D^{20°}$ − 6° (in water, c = 0·13). The sign of rotation was reversed in 10% hydrochloric acid. It gave the typical red colour with benzoquinone. On oxidation with chloramine-T it gave *iso*valeraldehyde, which was isolated as the p-nitrophenylhydrazone, m. p. 115° (after crystallisation from dilute alcohol). Leucine, similarly treated, gave the p-nitrophenylhydrazone, m. p. 115°. The mixed m. p. was the same. Wooley and Peterson (*J. Biol. Chem.*, 1936, **114**, 88) give m. p. 108°.

Action of Heat.—Ergotoxine and ergotinine give crystalline sublimates of *iso*butyrylformamide on pyrolysis at atmospheric pressure (Barger and Ewins, J., 1910, **97**, 284). Ergosinine, heated in precisely the same way, gave no crystalline sublimate.

Ergosinine (1 g.) was heated at 210—230°/3—4 mm. in a small flask with a long neck. Immediately above the bulb 4 inches of the neck were surrounded by a steam jacket, leaving a length of about 6 inches, which was kept cool by surrounding it with filter-paper moistened with alcohol, to condense a sublimate (B). A partly crystallised gum (A) condensed inside the steam jacket and the ergosinine was heated for 25 minutes to give the best yield. The product was dissolved in chloroform, treated with charcoal, filtered, and evaporated to dryness, giving a hard, light brown gum (0·37 g.). This was redistilled at 3—4 mm. (oil-bath at 200—220°). The light yellow, semi-crystalline solid was triturated with ether and yielded a white semi-crystalline solid, which was recrystallised from ethyl acetate until it gave well-formed rods of constant m. p., 148°. The mother-liquors yielded two crystalline white substances, (a) m. p. 125° and (b) m. p. 170°, which were not further purified. The pure compound (m. p. 148°) is very sparingly soluble in ether, easily soluble in alcohol, and less soluble in water, giving a neutral (litmus) solution; $[\alpha]_{5461}^{20}$ + 105° (approx., water, c = 1) (Found for material

dried at 80° in a vacuum: C, 63·1; H, 8·6; N, 13·2; *M*, Rast, 230. *Leucylproline lactam*, $C_{11}H_{18}O_2N_2$, requires C, 62·9; H, 8·6; N, 13·3%; *M*, 210).

Hydrolysis of l-*Leucyl*-d-*proline Lactam*.—The pure substance (70 mg.) was digested with concentrated hydrochloric acid (10 c.c.) for 19 hours in a steam-bath. The solution was evaporated to dryness, the residue freed from hydrochloric acid with silver sulphate, the free sulphuric acid removed with barium carbonate, and the solution evaporated to dryness. By trituration with alcohol the crystalline material (0·031 g.) remained out of solution. After recrystallisation it melted at about 290°, gave the benzoquinone colour reaction for leucine, and had $[\alpha]_D^{20°}$ − 11° (water, c = 2). The 3 : 5-dinitrobenzoyl derivative had m. p. 185°, not depressed by dinitrobenzoyl-leucine (Found for the substance dried at 100° in a vacuum: C, 48·1; H, 4·7; N, 12·8. Calc. for $C_{13}H_{15}O_7N_3$: C, 48·0; H, 4·6; N, 12·9%).

The alcohol-soluble fraction gave on evaporation a soft gum (0·036 g.), which had $[\alpha]_{5461}^{20°}$ + 62° (water, c = 1). This material gave the pine-wood reaction for proline and was very easily soluble in water. It was dissolved in water (2 or 3 c.c.), made just alkaline with dilute caustic soda solution, and shaken with methyl sulphate (0·2 c.c.) until the latter had passed into solution. Caustic soda solution was added when required to keep the solution alkaline. The solution was acidified with concentrated hydrochloric acid, and a slight excess of 10% solution of gold chloride added. The precipitate was recrystallised from 10% hydrochloric acid containing a trace of gold chloride. The crystals melted sharply at 245° (after sintering) when heated from 220° and gave $[\alpha]_{5461}^{20°}$ + 5° (approx. 2% HCl, c = 2) (Found for the substance dried at 80° in a vacuum: C, 17·5; H, 3·0; Au, 40·6; Cl, 29·2. Calc. for $C_7H_{13}O_2N,HAuCl_4$: C, 17·4; H, 2·9; Au, 40·8; Cl, 29·4%). A sample of the betaine aurichloride prepared from *l*-proline ($[\alpha]_{5461}^{20°}$ − 101°, water, c = 1) by the same technique melted similarly at 245° and had $[\alpha]_{5461}^{20°}$ − 14° (approx.). Evidently the *d*-proline from the lactam had partly racemised during the hydrolysis.

The sublimate (B), resublimed at 30—50°/3 mm., gave hard white needles, m. p. 115° to 125° according to the rate of heating. Pyruvamide could only be obtained in soft leaflets, though they showed a similar m. p. The analytical figures indicated a mixture. On warming with 10% sodium hydroxide solution, a strong ammoniacal smell was observed and the cooled solution after acidification with hydrochloric acid, followed by addition of ammonia and sodium nitroprusside, gave the typical blue colour for pyruvic acid.

Conversion of Ergosinine into Ergosine with Acid.—The base (10 g.) was boiled with acetone (90 c.c.), phosphoric acid (d 1·75, 2·5 c.c.), water (5 c.c.), and alcohol (10 c.c.) for 9 hours in an atmosphere of nitrogen. The mixture was diluted with water, concentrated under reduced pressure to remove the organic solvents, basified with sodium bicarbonate, and extracted with chloroform. The extract, after being dried over magnesium sulphate, was evaporated to dryness, and the residue crystallised twice from ethyl acetate. Yield, 1·0 g. (direct). Fractionation gave further quantities of ergosine and unchanged ergosinine.

Ergosine is readily soluble in chloroform, fairly readily soluble in methyl alcohol and acetone, sparingly soluble in ethyl acetate and benzene. It is less soluble in chloroform and much more soluble in methyl alcohol than ergosinine. It crystallised readily from ethyl acetate in prisms, m. p. 228° with blackening and frothing. It crystallises from methyl alcohol free from solvent. The specific rotations are: $[\alpha]_{5461}^{20°}$ − 193°, $[\alpha]_D^{20°}$ − 161° (in chloroform, c = 1); $[\alpha]_{5461}^{20°}$ + 24°, $[\alpha]_D^{20°}$ + 16° (in acetone, c = 1) (Found: C, 65·8; H, 6·8; N, 12·9%). Ergosine gives the typical blue colour with the dimethylaminobenzaldehyde reagent (*loc. cit.*) and, compared quantitatively with ergosinine, the colour intensities are approximately equal. It also gives the colour reactions mentioned under ergosinine.

The absorption spectrum measured in M/10,000 and M/30,000 solution in absolute alcohol is identical with that of ergosinine except that the inflexion at A. 2420 is less marked.

Conversion of Ergosinine into Ergosine with Alkali.—Ergosinine (1 g.) was dissolved in a mixture of *N*-alcoholic potash (50 c.c.) and water (50 c.c.) in an atmosphere of nitrogen, and the solution kept at the ordinary temperature for 45 minutes. It was then diluted with water, acidified with hydrochloric acid, and made alkaline with sodium bicarbonate, and the alkaloids exhaustively extracted with ether. After drying over sodium sulphate, the ethereal solution was evaporated to dryness. The solid gave a blue colour with dimethylaminobenzaldehyde approximately equal to that given by ergosinine. The solid was triturated with methyl alcohol to yield semi-crystalline ergosinine and the methyl-alcoholic filtrate was evaporated to dryness to give a residue which yielded crude ergosine by trituration with ethyl acetate. The ethyl acetate filtrate was evaporated; the residue again yielded crude ergosinine and ergosine by treatment with methyl alcohol and ethyl acetate. The total crude ergosinine

(0·41 g.) and ergosine (0·42 g.) had $[\alpha]_{5461}^{20^\circ}$ + 480° and $[\alpha]_{5461}^{20^\circ}$ – 40°, respectively (chloroform, *c* = 1). These rotations correspond to ergosinine–ergosine mixtures containing respectively 94% of ergosinine and 78% of ergosine, by calculation. They were purified by recrystallisation from 90% acetone and ethyl acetate, respectively, and then gave $[\alpha]_{5461}^{20^\circ}$ + 520° and $[\alpha]_{5461}^{20^\circ}$ – 194° (chloroform, *c* = 1) respectively (Found for the respective materials dried at 100° in a vacuum: C, 66·1; H, 6·9; N, 12·7; C, 66·0; H, 6·8; N, 13·0. Calc. for $C_{30}H_{37}O_5N_5$: C, 65·8; H, 6·8; N, 12·8%).

Ergosine Hydrochloride.—The base (0·1 g.), dissolved in acetone (5 c.c.), was treated with hydrogen chloride until the solution became acid. Diamond-shaped plates, m. p. 235° (decomp.), separated in a few minutes. The *hydrochloride* is moderately easily soluble in water, the solution is slightly acid, and the salt is precipitated in the amorphous state by the addition of hydrochloric acid. It crystallises in combination with acetone (Found: C, 62·2; H, 7·0; N, 10·7; HCl, 5·9. $C_{30}H_{37}O_5N_5$,HCl,$COMe_2$ requires C, 61·8; H, 6·9; N, 10·9; HCl, 5·7%).

Ergosine hydrobromide was prepared by the addition of 40% hydrobromic acid to a solution of the base in acetone. It crystallised in needles, which began to darken at 200° and decompose with blackening and frothing at 230°. It is moderately easily soluble in water, giving an acid solution from which it is precipitated in the amorphous condition by the addition of hydrobromic acid (Found for the crystals: C, 57·7; H, 6·3; N, 10·4; HBr, 12·0. $C_{30}H_{37}O_5N_5$,HBr,$COMe_2$ requires C, 57·7; H, 6·4; N, 10·2; HBr, 11·8%).

Ergosine nitrate was prepared by the addition of concentrated nitric acid, diluted with acetone, to a solution of the base in acetone. It crystallised in needles which began to darken at 185° and decompose at 215°. It is moderately easily soluble in water, giving an acid solution, from which the amorphous salt is precipitated on the adddition of nitric acid (Found for the crystals: C, 59·2; H, 6·4; N, 12·9; HNO_3, 9·6. $C_{30}H_{37}O_5N_5$,HNO_3,$COMe_2$ requires C, 59·3; H, 6·6; N, 12·6; HNO_3, 9·5%).

Ergosine methiodide was prepared by the addition of methyl iodide to a solution of the base in a little chloroform. It separated as an amorphous powder, which decomposed at 215° with previous darkening and could not be crystallised (Found: C, 53·7; H, 5·7; N, 10·2. $C_{30}H_{37}O_5N_5$,MeI requires C, 53·9; H, 5·8; N, 10·2%).

Ergosinine–Ergosine Molecular Compound.—Mixtures of ergosinine and ergosine in the proportions, respectively, of 2 to 3 and 3 to 2 were repeatedly crystallised from ethyl acetate. In each case a compound of constant optical rotation was obtained in small fine needles. The same substance was similarly obtained from chloroform, but less conveniently, owing to the easier solubility of the crystals. The crystals are less soluble in chloroform or ethyl acetate than either alkaloid. The crystals melted (decomp.) at about 200°. The material, dried at 100° in a vacuum, had $[\alpha]_{5461}^{20^\circ}$ + 164°; $[\alpha]_D^{20^\circ}$ + 128° (chloroform, *c* = 0·5) (Found: C, 66·0; H, 6·9; N, 12·8. $C_{30}H_{37}O_5N_5$ requires C, 65·8; H, 6·8; N, 12·8%). The constituents are separable by treating the crystals with methyl alcohol, ergosinine remaining undissolved.

We wish to acknowledge our indebtedness to Mr. J. E. Brooks for assistance in the practical work, to Mr. R. N. Fox for the measurement of the ultra-violet absorption spectra, and to Mr. A. Bennett and Mr. H. C. Clarke for the microanalyses.

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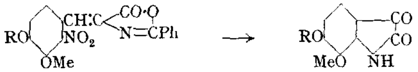
(*Addendum, March 5th*) Through the kindness of Prof. Barger we have been able to examine a specimen of ergoclavine supplied by Merck. It melted at 175° and had $[\alpha]_D^{20^\circ}$ + 130° (chloroform, *c* = 1) (Found: C, 65·8; H, 6·9; N, 12·5%). After three crystallisations from ethyl acetate the crystals closely resembled those of the ergosine–ergosinine complex, melted at the same temperature, and had the same elementary composition (Found: C, 65·8; H, 6·9; N, 12·6%). Treatment with methyl alcohol effected a separation into a sparingly soluble and a readily soluble fraction. These after crystallisation from aqueous acetone and ethyl acetate respectively gave ergosinine, m. p. 228°, $[\alpha]_{5461}^{20^\circ}$ + 520° (chloroform, *c* = 1) (Found: C, 65·9; H, 6·9; N, 12·8%), and ergosine, m. p. 228°, $[\alpha]_{5461}^{20^\circ}$ – 194° (chloroform, *c* = 1) (Found: C, 66·1; H, 6·8; N, 13·0%). These results leave no doubt that ergoclavine is a complex of ergosine and ergosinine, and the value for the optical rotation is that of an equimolecular mixture of the two.

Küssner (*Z. angew. Chem.*, **1937**, **50**, 34) also has recognised that his ergoclavine is a mixture of two alkaloids and has separated it into an alkaloid having $[\alpha]_D$ + 410°, m. p. 196°, and another, $[\alpha]_D$ – 149°, m. p. not given (both rotations in chloroform). These are no doubt ergosinine and ergosine incompletely purified.

84. *The Alkaline Hydrolysis of the Azlactones derived from Certain* o-*Nitrobenzaldehydes. The Formation of Isatins.*

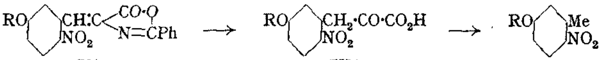
By HAROLD BURTON and JOHN L. STOVES.

GULLAND, ROSS, and SMELLIE (J., 1931, 2890) were unable to isolate homogeneous material when 5-keto-2-phenyl-4-(2′-nitro-4′-acetoxy-3′-methoxybenzylidene)-4 : 5-dihydro-oxazole (I; R = Ac) was hydrolysed with baryta, but they deduced the probable formation of an isatin from colour reactions. Their failure to isolate the isatin was probably due to the use of too small a quantity of the oxazolone, since we have had no difficulty in showing that 6-*hydroxy-7-methoxyisatin* (II; R = H) is formed in 60% yield when it is hydrolysed with 10% aqueous sodium hydroxide.

(I.)  (II.)

The new isatin is readily characterised through its sparingly soluble *semicarbazone.* The course of this oxidation–reduction reaction appears to differ slightly from that with 5-keto-2-phenyl-4-(2′-nitro-3′ : 4′-dimethoxybenzylidene)-4 : 5-dihydro-oxazole (I; R = Me)—which was shown by Gulland, Robinson, Scott, and Thornley (J., 1929, 2924) to be hydrolysed by aqueous-alcoholic sodium hydroxide to 6 : 7-dimethoxyisatin and 2-aminoveratric acid—since the formation of 2-amino-4-hydroxy-3-methoxybenzoic could not be proved. We have found that 6 : 7-dimethoxyisatin and 2-aminoveratric acid are also formed when the oxazolone (I; R = Me) is hydrolysed with 10% aqueous sodium hydroxide. The suggestion previously made (Burton, J., 1935, 1265) that the 2-aminoveratric acid results by intramolecular dismutation of the intermediate 2-nitrohomoveratrole has not been capable of experimental proof, since the amount of alkali-insoluble material formed during the hydrolysis with aqueous sodium hydroxide was too small to allow of identification. This negative result must not be considered to disprove the suggestion, since the amount of 2-aminoveratric acid isolated is relatively small, thus indicating that the concentration of the nitrohomoveratrole, if produced, must also be small.

We have shown, however, that 2-*nitro-5-benzyloxyphenylpyruvic acid* (III; R = CH_2Ph), which was synthesised from 2-nitro-5-benzyloxytoluene (IV; R = CH_2Ph) and ethyl oxalate in the presence of potassium ethoxide, is rapidly converted by boiling 10% aqueous sodium hydroxide into 2-nitro-5-benzyloxytoluene, thus affording strong evidence that the hydrolysis of the oxazolones of type (V) previously studied (Burton, *loc. cit.*) probably occurs in the following way:



(V.) (III.) (IV.)

It is not unlikely that the hydrolysis of the oxazolones (I; R = Ac or Me) also gives the corresponding *o*-nitrophenylpyruvic acids, which, owing to some structural feature, undergo an oxidation–reduction process to give 6-hydroxy-7-methoxy- and 6 : 7-dimethoxyisatin respectively (compare Reissert, *Ber.*, 1897, **30**, 1036). The structural feature in question is probably the presence of a substituent adjacent to the nitro-group rather than to the presence of two substituents in addition to nitro, since Oliverio (*Gazzetta*, **1935**, **65**, **143**) has shown that 5-keto-2-phenyl-4-(2′-nitro-4′ : 5′-dimethoxybenzylidene)-4 : 5-dihydro-oxazole reacts in the same manner as (V) to give 6-nitrohomoveratrole but no isatin.

EXPERIMENTAL.

6-*Hydroxy-7-methoxyisatin* (II; R = H).—9·55 G. of 5-keto-2-phenyl-4-(2′-nitro-4′-acetoxy-3′-methoxybenzylidene)-4 : 5-dihydro-oxazole, m. p. 171—172° (Found: C, 59·4; H, 3·7. Calc. for $C_{19}H_{14}O_7N_2$: C, 59·7; H, 3·7%), prepared from 2-nitroacetylvanillin (Slotta and

Lauerson, *J. pr. Chem.*, **1934**, **139**, 220) and hippuric acid by Gulland, Ross, and Smellie's method (*loc. cit.*), was boiled with 10% sodium hydroxide solution (150 c.c.) under reflux for 4 hours; ammonia was evolved after the first few minutes. The dark brown solution was cooled and acidified by a stream of sulphur dioxide. The precipitated material was collected, dried in a vacuum desiccator, and extracted with boiling benzene. This treatment removed benzoic acid and left a dark-coloured amorphous material, which was warmed with moderately concentrated hydrochloric acid; the acidic extract did not give a dye when treated successively with nitrous acid and alkaline β-naphthol.

The filtrate after removal of the above precipitate containing benzoic acid was mixed with an excess of concentrated hydrochloric acid and boiled to expel all the sulphur dioxide, and the cooled solution filtered from a small amount of tarry matter and extracted four times with ether. The dried extract (sodium sulphate) afforded 2·9 g. (60% yield) which, recrystallised twice from a small amount of glacial acetic acid, gave the *isatin* in dark red needles, m. p. 246—247° (decomp.) (Found: C, 56·0; H, 3·8; N, 7·15. $C_9H_7O_4N$ requires C, 55·95; H, 3·6; N, 7·25%), readily soluble in water and alcohol but much less soluble in chloroform, benzene, and ether. The *semicarbazone* separated in golden-yellow plates when a solution of the isatin in alcohol was mixed with aqueous semicarbazide acetate; it was insoluble in all the usual solvents except hot glacial acetic acid (from which it did not separate). When heated, it darkened gradually but had not melted at 270° (Found: N, 20·5, 20·6. $C_{10}H_{10}O_4N_4,H_2O$ requires N, 20·9%).

6 : 7-*Dimethoxyisatin and* 2-*Aminoveratric Acid.*—A mixture of 5-keto-2-phenyl-4-(2′-nitro-3′ : 4′-dimethoxybenzylidene)-4 : 5-dihydro-oxazole (8·85 g.) and 10% sodium hydroxide solution (100 c.c.) was boiled under reflux for 3½ hours. A little steam-volatile oil was formed, but extraction of the dark red solution with ether after 1 hour removed less than 0·2 g. of a yellow oil (? 2-nitrohomoveratrole). Benzoic acid, 2-aminoveratric acid (0·4 g.), m. p. 184° after crystallisation from water, and 6 : 7-dimethoxyisatin (2·2 g.), m. p. 212—213° after crystallisation from alcohol, were isolated from the hydrolysate by Gulland, Robinson, Scott, and Thornley's procedure (*loc. cit.*).

6-*Nitro*-m-*cresol.*—Blaikie and Perkin's method (J., 1924, **125**, 307) of preparation led, in our hands, to unworkable tarry products. The following procedure proved satisfactory. Acetyl nitrate, prepared from nitric acid (*d* 1·5; 47 g.) and acetic anhydride (110 g.) below 0°, was added slowly with stirring to a solution of *m*-cresol (65 g.) in acetic anhydride (171 g.) at − 5°; the mixture was then kept for 6 hours, poured on ice, and left overnight. Steam-distillation of the nitrated product removed 4-nitro-*m*-cresol (23 g.); on cooling, the non-volatile residue solidified to a dark crystalline mass. Recrystallisation of this from benzene gave 16 g. of 6-nitro-*m*-cresol, m. p. 125—126°, which was sufficiently pure for the preparation of its benzyl ether.

2-*Nitro*-5-*benzyloxyphenylpyruvic Acid* (III; R = CH_2Ph).—Potassium ethoxide from powdered potassium (6·6 g.) and sodium-dried alcohol (7·7 g.) in ether (250 c.c.) was treated with ethyl oxalate (26 g.) and then with 2-nitro-5-benzyloxytoluene (41 g. dissolved in the minimum amount of ether). The mixture was heated under reflux for 18 hours, water added to dissolve the solid which separated, and the aqueous extract acidified (Congo-red) with concentrated hydrochloric acid. The *pyruvic acid* separated as a red oil which gradually solidified (yield, 22 g.). Recrystallisation from water gave pale yellow needles, m. p. 103°, containing water of crystallisation (Found: C, 59·8; H, 4·7; N, 4·3. $C_{16}H_{13}O_6N,\frac{1}{2}H_2O$ requires C, 59·3; H, 4·3; N, 4·3%). A dilute alcoholic solution of the acid gave a deep green coloration with ferric chloride.

The acid was also prepared with sodium ethoxide as the condensing agent, but was obtained in a less pure condition. The reduction of the acid to 5-benzyloxyindole-2-carboxylic acid is reserved for a future communication dealing with the synthesis of various derivatives of indole.

Conversion of 2-*Nitro*-5-*benzyloxypyruvic Acid into* 2-*Nitro*-5-*benzyloxytoluene.*—A solution of the acid (3·25 g.) in 10% sodium hydroxide solution (30 c.c.) was boiled under reflux for 1 hour; oil separated after the first few minutes. Extraction with ether removed 1·7 g. (70% yield) of 2-nitro-5-benzyloxytoluene, m. p. 72—73° (after crystallisation from alcohol) either alone or mixed with an authentic specimen.

The University, Leeds. [*Received, January 6th*, **1937**.]

85. *Rearrangement of the Alkylanilines. Part VII. The Behaviour of Alkylanilines with* tert.*-Alkyl Groups.*

By W. J. Hickinbottom.

In earlier papers (J., 1931, 1281; 1932, 2396) evidence was adduced to support the view that, if hydrogen halides are used as promoters, the rearrangement of alkylanilines containing alkyl groups higher than propyl is due largely to the elimination of the alkyl group as olefin. Subsequent reaction of the olefin with the aromatic nucleus furnishes the so-called rearrangement product.

A detailed examination of the reaction of olefins with arylamines has shown that the products are of two types, (1) a secondary amine, resulting from the saturation of the olefinic linkage by the amino-group, and (2) an aminoalkylbenzene, which has been considered to be formed by combination of the olefin with the aromatic nucleus (J., 1932, 2646; 1934, 319, 1981; 1935, 1279). The following table summarises some of the results obtained, and it is clear that, under conditions comparable with those obtaining in the rearrangement, the yields of secondary amine are small; only under specially favourable conditions, notably the use of an excess of arylamine, can any appreciable amount of secondary amine be obtained. Octene is the only exception to these generalisations, and it will be referred to in a subsequent paper.

In an earlier communication the deduction was made, from a number of considerations, that the aminoalkylbenzene is produced by the direct reaction of the olefin with the nucleus of the aromatic amine rather than by rearrangement of the secondary amine. Support for this view is afforded by the known difficulty of forming a secondary amine by saturating the double bond of an olefinic hydrocarbon by an amino-group. Indeed, except for the examples referred to in the table, no other authentic examples of such a reaction are known to the author.

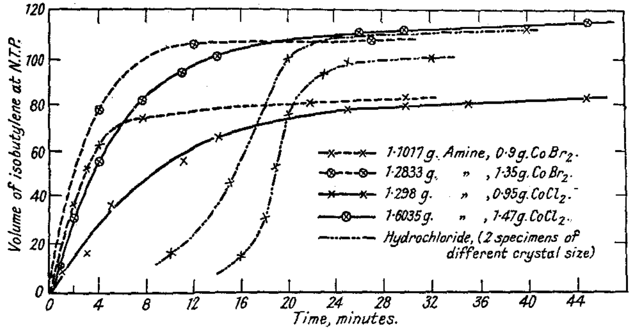
Aniline, g.	Promoter.	G.	Olefin.	G.	Temp.	Hours.	Yield of amine, g. Secondary.	Primary.
80	NH_2,Ph,HCl	10	$CMe_2{:}CH_2$	5	220—240°	22	0·61	1·45
30	NH_2Ph,HBr	1	$CMe_2{:}CHMe$	6	230—250	6	0·51	1·80
30	NH_2Ph,HBr	3	,, ,,	6	230—250	6·5	0·57	3·7
40	NH_2Ph,HBr	4	,, ,,	7·1	240—260	5·5	1·84	3·3
100	NH_2Ph,HCl	6	,, ,,	12	240—260	25	0·59	6·85
100	$(NH_2Ph)_2,CoCl_2$	8	,, ,,	14·5	245	24	0·37	2·71
50	NH_2Ph,HCl	4	CMeEt:CHMe	10·5	230—270	5	1·7	2·7
6	NH_2Ph,HCl	3	,, ,,	3·5	285—290	3·5	trace	1·02
50	NH_2Ph,HCl	8	$CEt_2{:}CHMe$	10	230—260	12	0·35	1·22
5	NH_2Ph,HCl	2	$CHPh{:}CH_2$	5	270	6	trace	3·50
40	NH_2Ph,HCl	8	,, ,,	10·8	200—240	6	0·68	5·26
50	$(NH_2Ph)_2,CdCl_2$	7·7	,, ,,	7·2	235	24	0·09	0·94
50	$(NH_2Ph)_2,CoCl_2$	5·6	,, ,,	9·1	240	24	0·3	0·69
7·2	NH_2Ph,HBr	13·3	$C_{10}H_{10}$*	9·9	220	6	nil	9·8
40	NH_2Ph,HCl	12	Δ^{α}- and Δ^{β}-Octenes	7·2	210—240	24	1·0	0·1

* *Dihydronaphthalene.*

In order to submit these views to further investigation, particularly to ascertain if any serious amount of primary amine could be formed from the secondary by rearrangement under the conditions employed, some of the alkylanilines produced by the addition of aniline to olefins have been heated with cobalt halides or as their hydrogen halide salts, under conditions which normally bring about rearrangement (Hickinbottom, J., 1927, 64; 1932, 2398; Hickinbottom and Preston, J., 1930, 1569), in such a way that the olefin formed could be easily removed from the reaction mixture before undesirable secondary reactions could take place. This condition restricted the choice of suitable secondary amines to those which could yield a readily volatile olefin. For this reason, most of the experimental work was carried out with *tert.*-butylaniline, which has the advantage of permitting a simple and rapid measurement of the rate of decomposition.

When *tert.*-butylaniline is heated at 212° with anhydrous cobalt chloride or bromide, aniline is formed owing to the elimination of the *tert.*-butyl group as *iso*butylene. The rate

of evolution depends, *ceteris paribus*, on the concentration of the metal halide. This is shown in the figure, which records the volume of *iso*butylene at N.T.P. evolved from 1 g. of base with various amounts of catalyst. The product left after heating consisted largely of aniline and the cobalt halide with some unchanged secondary amine. The amount of *p*-amino-*tert*.-butylbenzene isolated was 0·7% of the weight of aniline present. The approximate accuracy of this assay was confirmed by analyses of the primary amines from two other decompositions, the results of which gave 1·7% of *p*-amino-*tert*.-butylbenzene in the product. With *tert*.-hexylaniline, similar results were obtained by heating with cobalt halides: a rapid evolution of γ-methyl-Δ^{β}-pentene and the formation of aniline. Although it was not possible to isolate any rearrangement product owing to the relatively small amount of starting material, analyses of the primary amine from two decompositions gave 3·7 and 1·7% of



rearrangement product. The decomposition of *tert*.-butylaniline hydrochloride at 212° followed the same course as with cobalt halides, namely, the rapid evolution of *iso*butylene.

It is clear that both *tert*.-butylaniline and *tert*.-hexylaniline suffer extensive decomposition when heated with cobalt halides or as hydrochloride, and the amount of rearrangement is quite insufficient to account for the yields of *p*-amino-*tert*.-butyl- or -hexyl-benzene obtained by reaction of *iso*butylene or γ-methyl-Δ^{β}-pentene with aniline. This is held to afford support for the view already expressed that the formation of aminoalkylbenzenes from olefins is due to the direct reaction of the olefin with the aromatic nucleus.

Experimental.

Thermal Decomposition of tert.*-Butylaniline*.—(a) *With metal salts*. *tert*.-Butylaniline (7 g.) and anhydrous cobalt chloride (3·5 g.) were heated together at 212° for 45 minutes in a long narrow tube with a bulb blown at the lower end. During the first 10 minutes there was a vigorous evolution of gas; thereafter the tube contained a considerable amount of dark blue solid. The gas was collected in chloroform, cooled in ice, to which a concentrated solution of bromine in chloroform was added gradually so that it remained faintly coloured. After ½ hour the chloroform solution was distilled, giving a small fraction, b. p. *ca*. 90°, and a main fraction, b. p. 146—149°, consisting of *iso*butylene dibromide. The dark blue solid, on decomposition with ammonia, yielded a mixture, which was separated into primary and secondary amines by treatment with aqueous zinc chloride. The primary amine consisted largely of aniline (b. p. and acetyl derivative), and a small residue of somewhat higher b. p. remained. From this, by conversion into acetyl derivative and subsequent crystallisation, 0·022 g. of *p*-acetamido-*tert*.-butylbenzene (m. p. 160—164°) was isolated, which, after further purification, was identified by m. p. and mixed m. p. This corresponds to a yield of 0·017 g. of *p*-amino-*tert*.-butylbenzene. The yield of aniline was 2·49 g. The secondary amine consisted of unchanged *tert*.-butylaniline (1·51 g.).

The volume of butylene evolved in this decomposition was determined by attaching the top

of the reaction tube to an azotometer. When the heating had been continued for the requisite period, the apparatus was swept out by a current of carbon dioxide. The *iso*butylene was then determined by absorption in bromine water. The results are summarised below.

Butylaniline, g.	Metal salt, g.		Duration of heating, mins.	Vol. of butylene, c.c.	Yield of butylene, %.
1·0077	$CoCl_2$	0·7	30	92·8	61·7
1·1017	$CoBr_2$	0·9	30	82·3	54·8
1·2833	$CoBr_2$	1·35	30	107·5	71·6
1·2980	$CoCl_2$	0·95	55	91·1	60·7

The rearrangement of *tert.*-butylaniline (8·45 g.) and anhydrous cobalt chloride (3·4 g.) at 212° for 13 hours gave 3·97 g. of aniline and 0·08 g. of crude *p*-acetamido-*tert.*-butylbenzene (m. p. 160—163°). The yield of rearrangement product is 1·6% of the weight of aniline formed.

No increase in the proportion of rearrangement product was observed if the temperature was raised. In one such experiment, *tert.*-butylaniline (8·88 g.) and cobalt chloride (3·60 g.) were heated at 237°. After 20 hours there was a slight evolution of ammonia owing to the formation of some diphenylamine. The reaction was therefore stopped at this stage. The product consisted of aniline, 4·99 g.; diphenylamine, 0·05 g.; other secondary and tertiary amines, 0·16 g.; *p*-amino-*tert.*-butylbenzene, 0·02 g. The yield of rearrangement product is 0·45% of the weight of aniline formed.

(b) *Decomposition of* tert.*-butylaniline hydrochloride.* The heating was effected under conditions similar to those described above. On heating at 212° the crystals decrepitate, then gradually soften, and an effervescence sets in with a steady evolution of a gas which was identified as *iso*butylene.

After 30—60 mins.' heating, the residue was found to consist of aniline hydrochloride with some unchanged *tert.*-butylaniline hydrochloride. It was not possible to detect with certainty the presence of *p*-amino-*tert.*-butylbenzene; if it is formed, the amount must be very small. The results are summarised below, the rate of evolution of butylene being recorded in the figure.

Butylaniline hydrochloride, g.	Heating at 212°, mins.	Vol. of butylene at N.T.P., c.c.	Yield of butylene, %.	Loss of HCl during heating, g.	Loss of HCl during heating, as % of butyl group evolved as C_4H_9Cl.
0·7563	60	not determined		0·0029	2·0
0·3754	45	30·4	67·1	—	—
0·4802	32	37·0	63·7	0·0036	3·1
0·8667	45	79·1	75·6	not determined	

Thermal Decomposition of tert.*-Hexylaniline.*—*tert.*-Hexylaniline (3·74 g.) and anhydrous cobalt bromide (4 g.) were heated at 212° for 2 hours. After about ½ hour the metal bromide had swollen so that the contents of the tube appeared free from liquid. The volatile product (1·33 g.), b. p. 67—68°, had all the characteristics of an olefin (γ-methyl-Δ^{β}-pentene boils at 68°). The residue after the reaction gave 0·05 g. of unchanged secondary amine. The primary amine consisted essentially of aniline (b. p. and acetyl derivative). The amount of rearrangement product was determined by evaporating the primary amine with hydrochloric acid and drying the residue to constant weight. Determination of the hydrogen chloride in the dry salt gave HCl, 27·74%, which is equivalent to 3·7% of *p*-amino-*tert.*-hexylbenzene.

In a further experiment, 3·37 g. of *tert.*-hexylaniline and 4 g. of anhydrous cobalt chloride, heated together for 2½ hours at 212°, gave 0·25 g. of unchanged secondary amine, and a primary amine which consisted almost entirely of aniline. Analysis of the dried hydrochloride of the primary amine gave HCl, 27·93%, corresponding to 1·6% of *p*-amino-*tert.*-hexylbenzene.

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86. *Studies in the Sterol Group. Part XXIX. The Constitution of the Isomeric Ethers of Cholesterol.*

By J. H. BEYNON, I. M. HEILBRON, and F. S. SPRING.

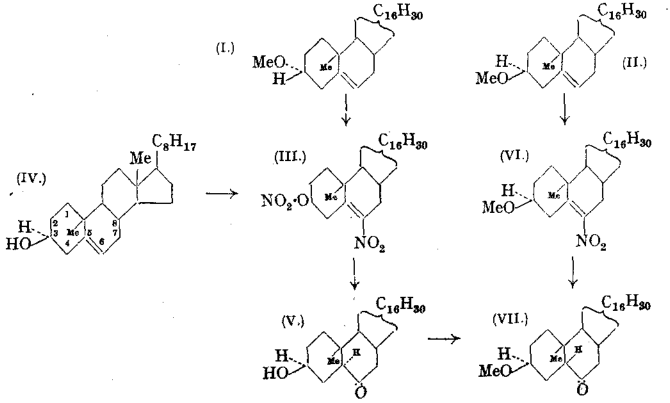
IN Part XXV (*J.*, 1936, 907) we reported that the isomeric pairs of cholesteryl methyl, ethyl, and benzyl ethers show remarkable differences in their reactions with the halogen acids and with bromine. For instance, the dextrorotatory or "*cis*" series of ethers yield

the corresponding cholesteryl halide and tribromocholestane respectively, whereas the lævorotatory or " *trans* " series fail to react with the halogen acids, and with bromine yield the corresponding ether 5 : 6-dibromides.

We now find that " *cis* "-cholesteryl methyl ether gives tribromocholestane with bromine in the presence of excess of potassium acetate, thus showing that the replacement of the methoxyl by bromine is not due to the catalytic influence of hydrogen bromide. Furthermore, " *cis* "-cholesteryl methyl ether is quantitatively converted into cholesteryl acetate on refluxing with potassium or zinc acetate in acetic acid, and into cholesteryl chloride with acetyl chloride in pyridine solution; the " *trans* "-ether is unchanged under these conditions.

In order to examine the constitutional features responsible for the reactivity of the " *cis* "-cholesteryl ethers, it was decided to study the reactions of the saturated *cis*- and *trans*-cholestanyl methyl ethers. Whereas the latter reacts neither with bromine nor with halogen acids at room temperature, it was not possible to apply these reactions to the *cis*-ether, as all attempts to prepare it were unsuccessful. Thus the methylation of *cis*-cholestanol (Ruzicka, Brüngger, Eichenberger, and Meyer, *Helv. Chim. Acta*, 1934, **17**, 1407) by treatment of its potassium salt with methyl iodide was accompanied by epimerisation, with formation of *trans*-cholestanyl methyl ether. No reaction was observed when *cis*-cholestanol in benzene solution was heated under reflux with moist silver oxide and methyl iodide. With the same object, the hydrogenation of " *cis* "-cholesteryl methyl ether by the aid of a platinum catalyst was again studied, and contrary to the observations of Stoll (*Z. physiol. Chem.*, 1932, **207**, 147) and Wagner-Jauregg and Werner (*ibid.*, 1932, **213**, 119), gave in our hands a quantitative yield of cholestane, demethylation having accompanied the reduction process. The fact that the " *cis* "-ether gives cholestane and not coprostane provides further evidence in favour of the view previously expressed (Beynon, Heilbron, and Spring, *loc. cit.*) that the ethenoid linkage of the ether is situated between C_5–C_6 and not between C_4–C_5, as sterols of the latter (ψ-cholestene) type give coprostane derivatives on hydrogenation.

Further valuable information concerning the structural relationship of the two cholesteryl methyl ethers is obtained from an examination of their behaviour with nitric acid. Nitration of the " *cis* "-ether (I) yields 6-nitrocholesteryl nitrate (III), identical with that



prepared by the direct nitration of cholesterol (IV) (Windaus, *Ber.*, 1903, **36**, 3752). Nitration of " *trans* "-cholesteryl methyl ether (II), on the other hand, yields *6-nitro-3-methoxy-*

Δ^5-*cholestene* (VI), which on reduction with zinc dust and acetic acid is converted into 3-*methoxycholestan*-6-*one* (VII), identical with the ether prepared by methylation of 6-ketocholestanol (V), which in its turn is obtained by reduction of (III) with zinc and acetic acid (Windaus, *loc. cit.*).

This series of reactions locates the ethenoid linkage in the two cholesteryl ethers at C_5–C_6, and it therefore follows that they differ only in the orientation of the groups associated with C_3, *i.e.*, that they are correctly named as "*cis*"- and "*trans*"-3-methoxy-Δ^5-cholestenes.*

Experimental.

Cholesteryl Acetate from "cis"-*Cholesteryl Methyl Ether*.—A solution of "*cis*"-cholesteryl methyl ether (1 g.) and zinc acetate (2 g.) in glacial acetic acid (50 c.c.) was refluxed for 8 hours. The solid separating on dilution with water was crystallised from ethyl acetate, from which cholesteryl acetate (1 g.) separated in needles, $[\alpha]_D^{19°} - 30{\cdot}0°$ ($l = 1$, $c = 2{\cdot}4$),† m. p. 115°, unchanged by admixture with an authentic specimen.

Cholesteryl Chloride from "cis"-*Cholesteryl Methyl Ether*.—The ether (1 g.) was refluxed for 7 hours with acetyl chloride (50 c.c.) in dry pyridine (50 c.c.). The mixture was diluted with water, and the separated solid crystallised from acetone (charcoal), yielding cholesteryl chloride (1 g.) in laminæ, m. p. 95°, showing no depression on admixture with an authentic specimen.

trans-*Cholestanyl Methyl Ether*.—*cis*-Cholestanol (2 g.) was refluxed for 1 hour with a suspension of "molecular" potassium (0·5 g.) in dry benzene (30 c.c.). Methyl iodide (6 c.c.) was added, and the mixture refluxed for a further 3 hours. After the addition of alcohol, the solvent mixture was removed under reduced pressure, and the residual oil extracted with ether. Removal of the ether from the dried extract, followed by crystallisation of the residue from methyl alcohol, gave *trans*-cholestanyl methyl ether (2 g.) as plates, m. p. 83°, unchanged by admixture with an authentic specimen; $[\alpha]_D^{20°} + 19{\cdot}8°$ ($l = 1$, $c = 1{\cdot}78$) (Found : C, 83·6; H, 12·4. Calc. for $C_{28}H_{50}O$: C, 83·5; H, 12·5%).

Hydrogenation of "cis"-*Cholesteryl Methyl Ether*.—A solution of the ether (5 g.) in glacial acetic acid (150 c.c.) was shaken with hydrogen for 4 hours at 65—70° in the presence of platinum oxide (1 g.). The solid (4·5 g.) separating from the filtered mixture was crystallised from methyl alcohol, giving cholestane (4 g.) in plates, m. p. 80°, not depressed by admixture with an authentic specimen; $[\alpha]_D^{19°} + 26{\cdot}6°$ ($l = 1$, $c = 0{\cdot}9$) (Found : C, 86·9; H, 12·6. Calc. for $C_{27}H_{48}$: C, 87·0; H, 13·0%).

Nitration of "cis"-*Cholesteryl Methyl Ether*.—A mixture of nitric acid (d, 1·53; 50 c.c.) and glacial acetic acid (20 c.c.) was added during 1 hour with stirring to a suspension of "*cis*"-cholesteryl methyl ether (5 g.) in glacial acetic acid (60 c.c.) maintained at 0°. The solid separating on dilution of the solution with water was crystallised from glacial acetic acid, from which 6-nitrocholesteryl nitrate (4 g.) separated in colourless needles, m. p. 128°, showing no depression on admixture with an authentic specimen (Found : C, 68·0; H, 9·4; N, 5·9. Calc. for $C_{27}H_{44}O_5N_2$: C, 68·0; H, 9·3; N, 5·9%).

6-*Nitro*-3-*methoxy*-Δ^5-*cholestene*.—Nitric acid (d 1·42; 30 c.c.) was added during ½ hour to a suspension of "*trans*"-cholesteryl methyl ether (10 g.) in glacial acetic acid at 0°. The mixture was stirred at room temperature until complete solution occurred (4 hours), and then set aside at − 10° overnight. The solid separating on dilution with water was well washed with water, and crystallised from methyl alcohol, giving 6-*nitro*-3-*methoxy*-Δ^5-*cholestene* (5 g.) in needles, m. p. 114° (Found : C, 75·4; H, 10·5; N, 3·1; OMe, 7·1. $C_{28}H_{47}O_3N$ requires C, 75·4; H, 10·6; N, 3·1; OMe, 7·0%).

3-*Methoxycholestan*-6-*one*.—(a) 6-Nitro-3-methoxy-Δ^5-cholestene (9 g.) was boiled under reflux for 12 hours with zinc dust (40 g.) and glacial acetic acid (100 c.c.). The solid separating on dilution with water was extracted with ether, the extract washed with water, and dried. Removal of the ether and crystallisation of the residue from methyl alcohol gave 3-*methoxycholestan*-6-*one* (7·5 g.) in needles, $[\alpha]_D^{19°} - 11{\cdot}2°$ ($l = 1$, $c = 1{\cdot}4$); m. p. 92° (Found : C, 80·6; H, 11·5. $C_{28}H_{48}O_2$ requires C, 80·7; H, 11·6%). The *oxime* separated as needles from methyl alcohol, m. p. 210° (Found : C, 78·0; H, 11·4; N, 3·3. $C_{28}H_{49}O_2N$ requires C, 77·9; H, 11·45; N, 3·2%).

* (*Note added in proof, March 9th*). Since the completion of this work Wallis, Fernholz, and Gephard (*J. Amer. Chem. Soc.*, 1937, **59**, 137) have described the preparation of an i-cholesterol, which they assert contains a *cyclo*propane bridge and not an ethylenic linkage. They further suggest that a close relationship exists between i-cholesterol and the "*cis*"-cholesteryl ethers. The possibility of such a relationship is being examined.

† All rotations recorded were measured in chloroform solution.

(b) A solution of 6-ketocholestanol (1 g.) in benzene (50 c.c.) was refluxed for 40 hours with moist silver oxide (5 g.) and methyl iodide (15 c.c.). After filtration, the solvent was removed under reduced pressure, and the residue crystallised from methyl alcohol, from which 3-methoxycholestan-6-one (0·8 g.) separated in needles, $[\alpha]_D^{19°}$ − 11·2° (l = 1, c = 0·896), m. p. 92° alone or in admixture with the specimen prepared by method (a).

We thank the Department of Scientific and Industrial Research for a Senior Research Award to one of us (J. H. B.), and Imperial Chemical Industries, Ltd., for a grant.

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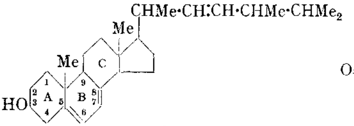
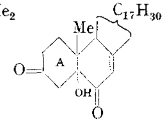
87. *Studies in the Sterol Group. Part XXX. The Oxidation of Ergosterol, Ergosteryl Acetate, and Lumisteryl Acetate with Chromic Anhydride.*

By A. BURAWOY.

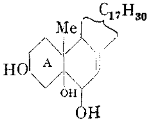
ALTHOUGH previous attempts to oxidise ergosterol (I) by means of chromic anhydride proved unsatisfactory (Reindel, *Annalen*, 1929, **466**, 136), reinvestigation of the reaction has shown that even under relatively drastic conditions a fair yield of ergostadiene-3 : 6-dion-5-ol (II) can be isolated. It is identical with that previously obtained by the oxidation of ergostadiene-3 : 5 : 6-triols-I and -II (III) (Heilbron, Morrison, and Simpson, J., 1933, 302; Dunn, Heilbron, Phipers, Samant, and Spring, J., 1934, 1576) and, as anticipated, it exhibits the characteristic selective absorption of an αβ-unsaturated ketone.



(I.)



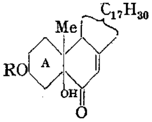
(II.)

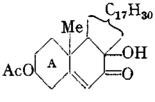


(III.)

Oxidation of ergosteryl acetate with the same reagent gives a neutral compound, $C_{30}H_{46}O_4$, m. p. 264°, which also exhibits the absorption spectrum of an αβ-unsaturated ketone. The Zerewitinoff method established the presence of one hydroxyl group, which is tertiary, since the compound is recovered unchanged after treatment with acetic anhydride. This fact clearly suggests that the compound is 3-*acetoxyergostadien*-6-*on*-5-*ol* (IV, R = Ac). An attempt to confirm this structure by converting the compound into the known ergostadiene-3 : 6-dion-5-ol (II) was unsuccessful, since on hydrolysis a mixture of acid and neutral products was obtained from which (IV, R = H) could not be isolated. That (IV) correctly represents the structure of the oxidation product was demonstrated by its reduction with aluminium *iso*propoxide, whereby ergostadiene-3 : 5 : 6-triol-II (III) was obtained, identical with that prepared by the oxidation of ergosterol with perbenzoic acid (Windaus and Lüttringhaus, *Annalen*, 1930, **481**, 127).

(IV.)





(V.)

In Part XXI (Heilbron, Spring, and Stewart, J., 1935, 1221) it was suggested that lumisterol differs from ergosterol only in the orientation of one or more of the asymmetric centres. Proof of the correctness of this view is to be found in the parallel behaviour of ergosteryl and lumisteryl acetates on oxidation with chromic acid. From the latter a 3-*acetoxylumi-*

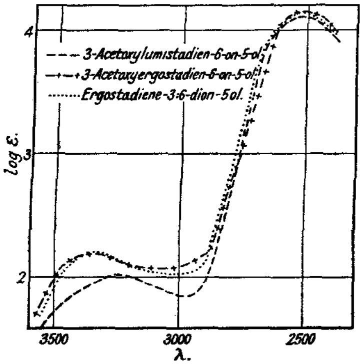
stadienonol is obtained which exhibits the typical absorption spectrum of an αβ-unsaturated ketone. That the hydroxyl group is tertiary and attached to a carbon atom adjacent to the carbonyl group is shown by the fact that oxidation of the lumistadienetriol-II monoacetate of Dimroth (*Ber.*, 1936, **69**, 1123) gives the same 3-acetoxylumistadienonol. Lumistadienetriol-II is, however, a stereoisomeride of lumistadienetriol-I (Heilbron, Moffet, and Spring, following paper), which has been shown to contain a tertiary-secondary α-glycol system in addition to the C_3-hydroxyl group (Heilbron, Spring, and Stewart, *loc. cit.*).

The characterisation of the primary products of oxidation of both ergosteryl and lumisteryl acetates not only establishes the identity of the conjugated system in the two sterols, but also confirms that this is located at C_5–C_6 and C_7–C_8. The conjugated ethenoid system of the two sterols must be in either ring B or ring C (Inhoffen, *Annalen*, **1932**, **494**, 116); of the four possible arrangements of the unsaturated system in these two rings, only the one indicated will allow of the formation of a hydroxy-αβ-unsaturated ketone in which the introduced hydroxyl group is tertiary and attached to a carbon atom adjacent to the carbonyl group. The constitution of the oxidation product from ergosteryl acetate has been shown to be (IV). The structure of 3-acetoxylumistadienonol, however, may be represented by either (IV) or (V); the decision between these structures is in favour of the former, since the absorption spectra of this compound and of 3-acetoxyergostadien-6-on-5-ol exhibit a band of high intensity at 2520 A. In contrast, sterol derivatives containing the chromophore of (V), such as 7-ketocholesteryl acetate, 7-ketositosteryl acetate, and 7-keto-Δ^5-cholestene,* are all characterised by a high-intensity band at 2350—2370 A.

Experimental.

Ergostadiene-3 : 6-dion-5-ol.—The oxidation was effected by addition of a solution of chromic acid (8·5 g.) in 90% acetic acid (55 c.c.) to ergosteryl acetate (10 g.) in acetic acid (300 c.c.) at 50°, the mixture being mechanically stirred. After 5 minutes the homogeneous solution was largely diluted with water, the precipitate filtered off, crystallised from alcohol, and recrystallised from benzene–alcohol, ergostadiene-3 : 6-dion-5-ol being obtained as plates, m. p. 249° (decomp.) either alone or in admixture with a specimen prepared by the method of Dunn, Heilbron, Phipers, Samant, and Spring (*loc. cit.*); yield, 20%. Identity of the two specimens was confirmed by a comparison of the corresponding oximes, m. p. 232—233°, either alone or in admixture; $[\alpha]_D^{20°}$ + 20° (l = 1, c = 1·16 in chloroform).

The absorption spectrum of chloroform solutions is shown in the figure: maxima, (*a*) 2520 A., ε = 13,450; (*b*) 3325 A., ε = 160.



3-Acetoxyergostadien-6-on-5-ol.—A suspension of ergosteryl acetate (10 g.) in acetic acid (200 c.c.) was treated with a solution of chromic acid (6·5 g.) in 80% acetic acid (24 c.c.), at 45°, the temperature rising to 80°. After 30 mins.' stirring, methyl alcohol (3 c.c.) was added, and the reaction mixture diluted with water. The solid separating was collected and crystallised successively from ethyl acetate, benzene, and ethyl acetate, from which *3-acetoxyergostadien-6-on-5-ol* separated in plates (yield 25%), m. p. 264° (decomp.), $[\alpha]_D^{21°}$ − 4·7° (l = 2, c = 0·90 in chloroform) (Found: C, 76·5; H, 9·7. $C_{30}H_{46}O_4$ requires C, 76·5; H, 9·8%); it does not give a semicarbazone. The absorption spectrum (chloroform solution) is shown in the figure: maxima, (*a*) 2515 A., ε = 13,570; (*b*) 3330 A., ε = 155.

* In contrast to this observation, Lettré and Inhoffen ("Über Sterine, Gallensäuren u.s.w.," p. 34) state that 7-keto-Δ^5-cholestene exhibits a maximum at 2480—2540 A.; this we cannot substantiate.

Active hydrogen determination (Zerewitinoff method). 15·76 Mg. of 3-acetoxyergostadien-6-on-5-ol evolved 0·84 c.c. of methane at 16° and 0·89 c.c. at 95°, corresponding to 1·12 and 1·18 atoms of active hydrogen per mole respectively.

Reduction of 3-Acetoxyergostadien-6-on-5-ol.—A solution of 3-acetoxyergostadien-6-on-5-ol (2·5 g.) and aluminium *iso*propoxide (10 g.) in *iso*propyl alcohol (400 c.c.) was heated under reflux for 52 hours. The mixture was concentrated to half bulk, diluted with water, and extracted with ether. The residue obtained by removal of the ether was repeatedly crystallised from ethyl acetate, from which the triol separated as prisms, m. p. 240°, undepressed on admixture with ergostadiene-3 : 5 : 6-triol-II. The triol does not exhibit selective absorption above 2400 A. (Found : C, 78·5; H, 10·8. Calc. for $C_{28}H_{46}O_3$: C, 78·1; H, 10·8%). The diacetate, prepared by refluxing the triol with acetic anhydride, separated from alcohol in prisms, m. p. 182° either alone or in admixture with ergostadiene-3 : 5 : 6-triol-II diacetate (Found : C, 75·0; H, 9·8. Calc. for $C_{32}H_{50}O_5$: C, 74·7; H, 9·8%).

3-Acetoxylumistadien-6-on-5-ol.—(a) A solution of lumisteryl acetate (9·5 g.) in acetic acid (200 c.c.) was oxidised at 45° with chromic acid (6·5 g.) in 80% acetic acid (60 c.c.) with mechanical stirring for 30 minutes. The solution was precipitated with water, extracted with ether, the ether removed, and the residue taken up in hot methyl alchol. The oil separating on cooling was isolated by decantation, and crystallisation effected from the same solvent, from which *3-acetoxylumistadien-6-on-5-ol* separated in prisms, m. p. 177—178°, $[\alpha]_D^{19°}$ + 11·7° (l = 1, c = 2·05 in chloroform) (Found : C, 76·5; H, 9·8. $C_{30}H_{46}O_4$ requires C, 76·5; H, 9·8%); yield, 15%. Light absorption in chloroform solution (see figure) : maxima, (*a*) 2515 A., ε = 13,130; (*b*) 3230 A., ε = 105.

(b) A solution of lumistadiene-3 : 5 : 6-triol monoacetate (1·9 g.) in acetic acid (30 c.c.) was treated with chromic acid (0·45 g.) in 80% acetic acid (22 c.c.) at room temperature, the mixture being mechanically stirred for 2 hours. After the addition of water, the separated solid was collected and crystallised from methyl alcohol, 3-acetoxylumistadien-6-on-5-ol (0·9 g.) being obtained in prisms, m. p. 177—178°, $[\alpha]_D^{19°}$ + 12·3° (l = 1, c = 1·78 in chloroform), identical with the preparation described under (a).

The author thanks Professor I. M. Heilbron, F.R.S., and Dr. F. S. Spring for their interest in this investigation, and acknowledges with gratitude grants from the Academic Assistance Council, London, and Imperial Chemical Industries, Ltd. (Dyestuffs Group).

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88. *Studies in the Sterol Group. Part XXXI. The Structure of Lumisterol.*

By I. M. HEILBRON, G. L. MOFFET, and F. S. SPRING.

IN Parts XXI and XXX (Heilbron, Spring, and Stewart, J., 1935, 1221; Burawoy, preceding paper) it has been established that lumisterol is a stereoisomeride of ergosterol. In further support of the structural identity of the two sterols we now find that lumisteryl acetate gives an *adduct* with maleic anhydride which, as in the case of the corresponding adduct from ergosteryl acetate, can be thermally decomposed with regeneration of its components.

In the hope of obtaining more precise information concerning the stereo-relationship of the two sterols we have now examined the fully saturated lumistanol. Lumistanyl acetate has previously been prepared by the catalytic hydrogenation of dihydrolumisteryl acetate (Ahrens, Fernholz, and Stoll, *Annalen*, 1933, **500**, 109), itself obtained by the reduction of lumisterol with sodium and ethyl alcohol (Windaus, Dittmar, and Fernholz, *Annalen*, 1932, **493**, 259). Although the direct catalytic hydrogenation of lumisteryl acetate was stated by the former authors to give an inseparable mixture, we have now succeeded in isolating both *lumistenyl acetate* (tetrahydrolumisteryl acetate), m. p. 179°, and lumistanyl acetate from the reaction mixture. Oxidation of lumistanol with chromic acid gives *lumistanone*, m. p. 121—122°, together with *lumistanedicarboxylic acid*, m. p. 208—210°. Although lumistanone is not identical with ergostanone (Reindel and Walter, *Annalen*, 1928, **460**, 222), it cannot be concluded that stereochemical differences other than the orien-

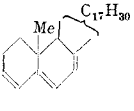
tation of the groups associated with C_3 exist between the two sterols, since it is conceivable that this alone would influence the spatial arrangement assumed by the ingoing hydrogens at the potentially asymmetric centres, C_5 and C_8.

In view of this complication it is apparent that a comparative study of ergosterol and lumisterol would be more profitably pursued by reference to their respective unsaturated derivatives.

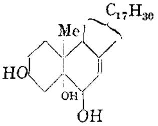
We have previously shown that dehydration of lumisterol with phosphorus oxychloride gives a lumistatetraene which differs from either of the ergostatetraenes A and B (Heilbron, Spring, and Stewart, *loc. cit.*). Lumistatetraene exhibits a well-defined absorption band at 3140 A., which by comparison with the principal band of lumisterol (max. 2790 A.) establishes the presence of three conjugated ethenoid linkages in the hydrocarbon, the structure of which must be (I). On the other hand, both the ergostatetraenes show a single-banded absorption spectrum with a maximum at 2600 A., showing that these hydrocarbons no longer contain the conjugated system of ergosterol.

In order to test the hypothesis that lumisterol is simply *epi*ergosterol, we attempted to oxidise the former to its ketone, reduction of which under specified conditions would lead to *epi*lumisterol. Although the oxidation of lumisterol with copper-bronze gives a *ketone*, m. p. 156—157°, this fails to exhibit the selective absorption characteristic either of lumisterol or of an αβ-unsaturated ketone which would result if the oxidation was accompanied by migration of the Δ^5-ethenoid linkage to the Δ^4-position (cf. cholestenone). A possible explanation of this anomaly is that the oxidation has been accompanied by a simultaneous saturation of the Δ^5-ethylenic linkage. The oxidation of dihydrolumisterol with copper-bronze, however, yields a *lumistadienone*, m. p. 175—176°, which differs from the ketone derived from lumisterol.

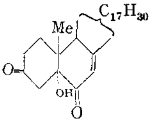
We next directed our attention to lumistadiene-3 : 5 : 6-triol-I (Heilbron, Spring, and Stewart, *loc. cit.*) and lumistadiene-3 : 5 : 6-triol-II (Dimroth, *Ber.*, 1936, **69**, 1123) (II). Each was oxidised with chromic acid, whereby one and the same *lumistadiene*-3 : 6-*dion*-5-*ol* (III), m. p. 182—183°, was obtained, a result which incidentally proves that the two triols are stereoisomeric, differing solely in the orientation of the C_6 hydroxyl groups.



(I.)



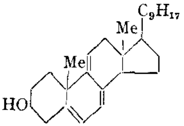
(II.)

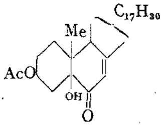


(III.)

The fact that lumistadiene-3 : 6-dion-5-ol differs from ergostadiene-3 : 6-dion-5-ol establishes either that asymmetric differences other than around C_3 exist between the two sterols, or that the two diketo-alcohols differ in the orientation of the hydroxyl group attached to C_5. The latter alternative is considered untenable in the light of the following *spectrographic observations.*

(IV.)





(V.)

Ergosterol and lumisterol, the chromophores of which are structurally the same, differ considerably in the intensity of their ultra-violet absorption. A similar difference is observed between dehydroergosterol and dehydrolumisterol (IV), such differences being common among stereoisomers ("Stereochemie," p. 746, Wassermann–Freudenberg, Leipzig, 1933). That these effects are not to be ascribed to the alternative orientation of

the C_3-hydroxyl group may be adduced from the observation that ergostadiene-3 : 6-dion-5-ol and lumistadiene-3 : 6-dion-5-ol (III) show the same persistent spectrographic differences in the low-intensity band, although in these diketones the C_3-centre of asymmetry has been removed. Further, the fact that lumistadiene-3 : 6-dion-5-ol and 3-acetoxylumistadien-6-on-5-ol (V) (Burawoy, *loc. cit.*) are spectroscopically indistinguishable, as are also the corresponding derivatives of the ergosterol series, demonstrates that neither the nature nor the orientation of the groups attached to C_3 contributes to the characteristic absorption of these αβ-unsaturated ketones.

	Ergo-		Lumi-	
	λ, max., A.	ε, max.	λ, max., A.	ε, max.
-sterol	2,815	12,000	2,790	8,500
Dehydro- -sterol (IV)	3,235	11,400	3,200	7,500
-stadienedionol (III)	2,525	13,450	2,530	13,500
	3,325	160	3,250	100
-stadienonediol monoacetate (V)	2,520	13,570	2,520	13,430
	3,330	155	3,230	105

The stereoisomerism responsible for the observed spectrographic differences between dehydrolumisterol and dehydroergosterol must therefore have its seat in C_{10}, which is directly adjacent to the chromophore. This difference in configuration around C_{10} must likewise exist between ergosterol and lumisterol. No information is available concerning the relative orientation of the hydroxyl groups and the C_9-hydrogen atoms of the two sterols.

Experimental.

Lumisteryl Acetate–Maleic Anhydride Adduct.—A mixture of lumisteryl acetate (0·5 g.) and maleic anhydride (0·3 g.) was heated for 30 minutes in an evacuated tube at 170—180°. The product was crystallised repeatedly from acetic anhydride, from which the *adduct* separated in plates, m. p. 176—177°, $[\alpha]_D^{22°}$ + 28·2° (l = 1, c = 2·13 in chloroform) (Found : C, 75·8; H, 9·1. $C_{34}H_{48}O_5$ requires C, 76·1; H, 9·0%); it distilled unchanged at 180°/3 × 10^{-4} mm., but on heating at 240°/15 mm. for 2 hours, followed by vacuum sublimation of the residue, lumisteryl acetate was obtained quantitatively.

Lumistenol.—A solution of lumisteryl acetate (5 g.) in glacial acetic acid (120 c.c.) was shaken with hydrogen and platinum oxide (0·5 g.) at 70—80°. After 5 hours the catalyst was removed, the solution cooled, and the separated solid collected and washed with acetic acid. Repeated crystallisation from alcohol gave *lumistenyl acetate* in plates, m. p. 178—179°, $[\alpha]_D^{20°}$ − 33·1° (l = 1, c = 1·51 in chloroform). Titration with perbenzoic acid proved the presence of one ethenoid linkage (Found : C, 81·5; H, 11·1. $C_{30}H_{50}O_2$ requires C, 81·4; H, 11·4%). Hydrolysis of the acetate with 5% methyl-alcoholic potash gave *lumistenol*, separating from aqueous alcohol in needles, m. p. 114—116°, $[\alpha]_D^{20°}$ − 0·5° (l = 1, c = 5·42 in chloroform) (Found : C, 83·8; H, 12·2. $C_{28}H_{48}O$ requires C, 83·9; H, 12·1%).

Lumistanol.—The acetic acid mother-liquor of lumistenyl acetate was diluted with water (30 c.c.), the solution clarified by warming, and slowly cooled, whereupon a second crop of impure lumistenyl acetate separated. Repetition of this process gave a third crop of lumistenyl acetate; further dilution of the mother-liquor with water resulted in the separation of oils. The solution was completely precipitated with water, extracted with ether, and the residue obtained after removal of the ether was hydrolysed by refluxing with 3% methyl-alcoholic potash (100 c.c.) for 2 hours. The product, isolated by means of ether, was repeatedly crystallised from acetone–alcohol (1 : 1), lumistanol being obtained in needles, m. p. 126—127°, $[\alpha]_D^{20°}$ + 8·2° (l = 1, c = 2·43 in chloroform).

Lumistanone and Lumistanedicarboxylic Acid.—A solution of lumistanol (1·5 g.) in glacial acetic acid (75 c.c.) was oxidised at 70° with a solution of chromic acid (1·0 g.) in acetic acid (85%; 8 c.c.), added during 1½ hours. The solution was stirred for a further 2 hours at the same temperature, and largely diluted with water. The product, isolated by means of ether, was separated into an acid and a neutral fraction by means of aqueous sodium carbonate. The neutral fraction (0·5 g.) separated in micro-needles from alcohol, and after repeated crystallisation from the same solvent had m. p. 121—122°, $[\alpha]_D^{22°}$ − 17·5° (l = 1, c = 3·97 in chloroform) (Found : C, 83·9; H, 11·8. $C_{28}H_{48}O$ requires C, 83·9; H, 12·1%). The *oxime* separated from alcohol in needles, m. p. 165—166° (Found : C, 80·8; H, 12·0; N, 3·4. $C_{28}H_{49}ON$ requires C, 80·9; H, 11·9; N, 3·4%).

The acid fraction from the oxidation mixture was crystallised repeatedly from dilute methyl alcohol, from which *lumistanedicarboxylic acid* separated in clusters of needles, m. p. 208—210°, $[\alpha]_D^{22°}$ + 24·6° (l = 1, c = 1·04 in chloroform) (Found : C, 74·7; H, 11·0. $C_{28}H_{48}O_4$ requires C, 74·9; H, 10·8%). The *dimethyl* ester, prepared by means of diazomethane, separated from dilute methyl alcohol in clusters of needles, m. p. 48—49° (Found : C, 75·2; H, 10·7. $C_{30}H_{52}O_4$ requires C, 75·6; H, 11·0%).

Lumistatetraene.—According as ergosterol is dehydrated with phosphorus oxychloride or with *p*-toluenesulphonyl chloride, two different hydrocarbons, ergostatetraene A and B, are obtained (Rygh, *Z. physiol. Chem.*, 1929, **185**, 99; Stoll, *ibid.*, 1931, **202**, 233). Furthermore, on refluxing with acetic anhydride, the tetraene A is isomerised to tetraene B. In the case of lumisterol, however, we find that dehydration by the latter reagent gives the same lumistatetraene as dehydration by the former reagent (Heilbron, Spring, and Stewart, *loc. cit.*). Lumisterol (1·0 g.) in pyridine (20 c.c.) was heated with *p*-toluenesulphonyl chloride (2·0 g.) for 30 minutes on the steam-bath. The cold mixture was diluted with water and extracted with ether, and the extract washed successively with dilute acetic acid, aqueous sodium carbonate, and water. The residue obtained by removal of the solvent from the dried solution was repeatedly crystallised from ether–methyl alcohol, from which lumistatetraene separated in long needles, m. p. 88°, either alone or in admixture with the phosphorus oxychloride preparation.

Lumistadiene-3 : 6-dion-5-ol.—A solution of lumistadiene-3 : 5 : 6-triol-I or -II (2·5 g.) in glacial acetic acid (190 c.c.) was treated with chromic anhydride (1·5 g.) in acetic acid (20 c.c.) and water (2 c.c.), added during an hour at room temperature with stirring. The stirring was continued for a further 1½ hours; the solution was then diluted with water and extracted with ether. The neutral fraction of the product, isolated in the usual manner, was crystallised from methyl alcohol, *lumistadiene-3 : 6-dion-5-ol* separating in clusters of needles, m. p. 182—183° (Found : C, 78·3; H, 10·2. $C_{28}H_{42}O_3$ requires C, 78·8; H, 9·9%).

Oxidation of Lumisterol with Copper-bronze.—An intimate mixture of lumisterol (5·6 g.) and copper-bronze was distilled under 5—6 mm. The fraction distilling at 245° (bath temp. 300—310°) (4 g.) solidified, and after repeated crystallisation from acetone the *ketone* separated in prisms, m. p. 156—157°, $[\alpha]_D^{22°}$ + 5·5° (l = 1, c = 1·37 in chloroform) (Found : C, 85·3; H, 11·3. $C_{28}H_{42}O$ requires C, 85·2; H, 10·7. $C_{28}H_{44}O$ requires C, 84·8; H, 11·2%). The 2 : 4-*dinitrophenylhydrazone* separated from alcohol in orange needles, m. p. 204—205° (Found : C, 71·2; H, 8·3; N, 9·65. $C_{34}H_{46}O_4N_4$ requires C, 71·0; H, 8·1; N, 9·7%. $C_{34}H_{48}O_4N_4$ requires C, 70·7; H, 8·4; N, 9·7%). The *oxime* separated from alcohol in plates, m. p. 168—169° (Found : C, 81·8; H, 11·0; N, 3·4. $C_{28}H_{43}ON$ requires C, 82·0; H, 10·6; N, 3·4%. $C_{28}H_{45}ON$ requires C, 81·7; H, 11·0; N, 3·4%).

Lumistadienone.—A mixture of dihydrolumisterol (3·0 g.) and copper-bronze (2·3 g.) was distilled at 3—5 mm. The main fraction distilled at 220—240°, and after repeated crystallisation of this from acetone, *lumistadienone* was obtained in plates, m. p. 175—176°, $[\alpha]_D^{24°}$ + 31·6° (l = 1, c = 1·64 in chloroform) (Found : C, 85·3; H, 11·3. $C_{28}H_{44}O$ requires C, 84·8; H, 11·2%). The *oxime* separated from aqueous alcohol in needles, m. p. 210—212° (decomp.) (Found : C, 81·8; H, 11·2; N, 3·4. $C_{28}H_{45}ON$ requires C, 81·7; H, 11·0; N, 3·4%).

Our thanks are due to Messrs. James Woolley, Sons and Co., Ltd., for a scholarship which enabled one of us (G. L. M.) to participate in this investigation, also to Messrs. Joseph Nathan and Co., Ltd., for a gift of lumisterol, and to the Rockefeller Foundation for a grant.

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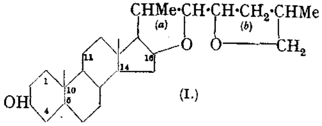
89. *Sapogenins. Part II. Sarsasapogenin and Smilagenin.*

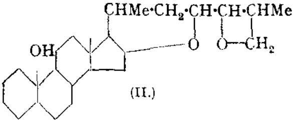
By STANLEY N. FARMER and GEORGE A. R. KON.

IT has been pointed out in Part I (Askew, Farmer, and Kon, J., 1936, 1399) that measurements of unimolecular films support formula (I), assigned to tigogenin by Tschesche and Hagedorn (*Ber.*, 1935, **68**, 1412, 2247; 1936, **69**, 797), but cannot be reconciled with the structure (II), tentatively put forward for sarsasapogenin by Jacobs and Simpson (*J. Biol. Chem.*, 1935, **109**, 501), in which the hydroxyl group is at position C_{11}. The surface area of sarsasapogenin was found to be somewhat greater than that of the isomeric tigogenin and

consistent with a hydroxyl either at C_2 or C_4 if the compound belongs to the cholestane series, or at C_3 if it is a coprostane derivative.



(I.)

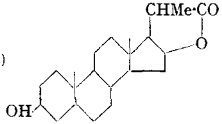


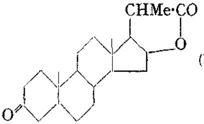
(II.)

The experiments now recorded establish that sarsasapogenin is a coprostane derivative, and that smilagenin, also described in Part I, only differs from it as regards the side chain. The position of the hydroxyl at C_3 receives further support from dehydrogenation experiments, and it is hoped to adduce final proof of it shortly.

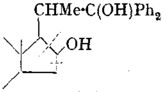
Sarsasapogenin acetate was oxidised with chromic acid to the *acetate* of the *lactone* (III); attempts to open the lactone ring with hydrogen bromide to afford a bromo-acid, which could be reduced to one of the known bile-acid derivatives, were unsuccessful, and we therefore carried out a degradation exactly analogous to that effected by Tschesche and Hagedorn (*Ber.*, 1935, **68**, 1412) on tigogenin. The lactone (III) was oxidised to the *keto-lactone* (IV), this reduced by Clemmensen's method to the deoxy-lactone, which was probably identical with the compound obtained by Jacobs and Simpson (*J. Biol. Chem.*, 1935, **110**, 565), and this treated with a large excess of phenylmagnesium bromide. The *diphenylcarbinol* (V) was oxidised to a mixture of the *acid* (VI) and ætiobilianic acid (VII), the latter in every way identical with a specimen kindly sent to us by Prof. H. Wieland.

(III.)

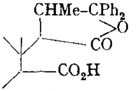




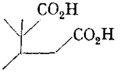
(IV.)



(V.)



(VI.)



(VII.)

The isolation of this acid proves that sarsasapogenin is a coprostane derivative; it also supplies an indication, though not a proof, that the hydroxyl cannot occupy position C_4, because the corresponding ketone would then be expected to undergo isomerisation with alkali. Treatment with acid causes degradation of the side chain, as found by Jacobs and Simpson, but the stability of the lactone (IV) under the conditions of the Clemmensen reduction is sufficient proof that this compound, in which the side chain has been shortened by oxidation, is stable to acids.

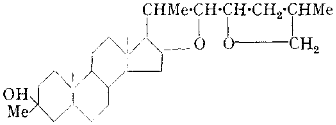
The opening of ring IV in the manner indicated shows that the oxide ring (*a*) must be attached to ring IV at C_{16}, as in tigogenin, and disposes of the alternative attachment to C_{15}, which was at one time regarded as a possibility by Jacobs and Simpson (*ibid.*).

We have established a connection between sarsasapogenin and smilagenin by oxidising the acetate of the latter to the acetate of the lactone (III), identical with that obtained from sarsasapogenin. It follows that the difference between these two aglucones must be confined to the last five carbon atoms of the side chain, which form part of the oxide ring (*b*) and are removed on oxidation to the lactone. It appears probable that the difference is one of configuration of the asymmetric carbon atom contained in this ring.

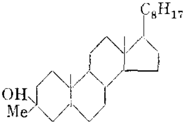
A by-product in the oxidation of smilagenin acetate is an acid, evidently analogous to the triketo-acid isolated by Jacobs and Simpson (*loc. cit.*) in their degradation of deoxysar-

sasapogenin. A similar, but apparently not identical, acid is also formed from sarsasapogenin acetate. In the formation of these acids the oxide rings are presumed to be broken and so the difference between the acids cannot be attributed to the steric configuration of the terminal oxide ring.

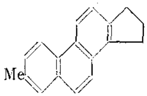
Apart, therefore, from the slight uncertainty regarding the nature of the side chain in these compounds, it only remains to establish the position of the hydroxyl group with certainty. It was hoped to do this by the selenium dehydrogenation of the methyl ether of sarsasapogenin to a methoxy-derivative of 3′-methyl*cyclo*pentenophenanthrene, but the required ether could not be prepared in sufficiently good yield. Sarsasapogenone was then treated with methylmagnesium iodide, and the resulting *methylsarsasapogenin* (VIII) dehydrogenated with selenium. The separation of the products, formed in poor yield, proved extremely difficult, but a hydrocarbon was eventually separated in the form of its *s*-trinitrobenzene *compound*, with the high m. p. of 174—175°, and this was in every way similar to a compound obtained by the same process starting with 3-*methylcholestan*-3-*ol* (IX), which was prepared for the sake of comparison. The identity of these compounds would establish the position of the methyl, and hence also the hydroxyl, group present in the starting materials.



(VIII.)



(IX.)



(X.)

The analysis of these derivatives appears to point to the parent hydrocarbon being a methyl*cyclo*pentenophenanthrene, presumably (X), in place of the expected dimethyl compound. However, the hydrocarbon regenerated from the apparently pure trinitrobenzene complex derived from methylcholestanol was not homogeneous, and a pure hydrocarbon has not yet been isolated. For this reason we prefer to leave the question of the nature of these dehydrogenation products open, pending the completion of synthetic experiments, now in progress together with a repetition of the dehydrogenation on a larger scale.

In our first experiment with methylcholestanol, the mixture of alcohol and selenium was gradually heated to 270°, then to 310—320°; hardly any dehydrogenation occurred under these conditions, and a saturated hydrocarbon, evidently *methylcholestane*, was recovered. This observation is analogous to that of Dorée and Petrov (J., **1934**, 1129; **1935**, 1391), who found that selenium could act as a hydrogenating catalyst in some cases. Methylcholestane was dehydrogenated by selenium at a higher temperature (350—360°).

We have continued our survey of the occurrence of smilagenin and sarsasapogenin, and have extracted a variety of sarsaparilla known as Jamaica red, said to be derived from *Smilax ornata* Hook. Except for its brick-red colour, the drug is outwardly very similar to the Jamaica grey variety; the yield of pure aglucone from it was extremely poor, in agreement with the low hæmolytic power of extracts of this drug noted by Kobert (*Pharm. J.*, 1912, **88**, 779), and the compound proved to be sarsasapogenin. The latter also occurs in Honduras sarsaparilla, because van der Haar (*Rec. trav. chim.*, 1929, **48**, 726) has isolated the same glucoside, parillin, from this and from Vera Cruz (Mexican) sarsaparilla, and hydrolysed it to a high-melting algucone; both these varieties of the drug may be derived from *Smilax medica* (" Encyclopædia Britannica," 11th Ed.).

EXPERIMENTAL.

Sarsasapogenin Methyl Ether.—An attempt to methylate sarsasapogenin with diazomethane was unsuccessful; a very poor yield of the desired product was obtained by the method of Heilbron and Simpson (J., 1932, 268). 2·5 G. of the genin were boiled under reflux with 25 c.c. of methyl iodide, 26 g. of precipitated and dried silver oxide, and 25 mg. of sodium hydroxide. The solid was filtered off, the solution washed and evaporated, and the residue crystallised from

acetone. The major part of the genin was recovered, but in the most soluble fraction another *compound* was present; after crystallisation from rectified spirit, it melted at 153—155° (Found: OMe, 7·7. $C_{28}H_{46}O_3$ requires OMe, 7·2%).

Oxidation of Sarsasapogenin Acetate.—41 G. of chromic acid, 25 c.c. of water, and 125 c.c. of acetic acid were heated on the steam-bath in a three-necked flask equipped with a stirrer, reflux condenser, and dropping-funnel. A solution of 23 g. of sarsasapogenin acetate (Askew, Farmer, and Kon, *loc. cit.*) in 900 c.c. of acetic acid was run in with constant stirring in the course of 5 hours, the mixture being then heated and stirred for a further 3 hours. The cooled solution was poured into 2 l. of water and repeatedly extracted with a large volume of ether. The extract was thoroughly washed with water to remove most of the acetic acid, then with sodium carbonate (extract A), water, sodium hydroxide (extract B), again with water, dried over sodium sulphate, and evaporated. The *acetate* of the lactone (III) remained as a nearly colourless residue; it was recrystallised from alcohol (yield 3·8 g., m. p. 181—183°) and was then pure enough for the next step. After three crystallisations from alcohol it formed small plates, m. p. 184·5° (Found: C, 74·0; H, 9·4. $C_{24}H_{36}O_4$ requires C, 74·2; H, 9·3%); it had $[\alpha]_D^{25°}$ − 32°, $[\alpha]_{5461}^{25°}$ − 40°, $[\alpha]_{5461}/[\alpha]_D$ 1·25 (c = 0·492 in chloroform).* The lactone dissolves in caustic alkali and is reprecipitated on acidification, but is evidently not extracted by alkali from its etheral solution.

The extract A was acidified with 10% sulphuric acid and extracted with ether. The dried extract gave on evaporation a gum; this was dissolved in ether and treated with a large excess of diazomethane. On removal of the ether a gum was obtained, which was dissolved in hot alcohol. Dense needles (590 mg.) were deposited on cooling in ice, m. p. 199—200° after another crystallisation from the same solvent. The compound was evidently the *methyl* ester of a triketo-acid (Found: C, 69·6; H, 8·9. $C_{30}H_{44}O_7$ requires C, 69·7; H, 8·6%), analogous to that isolated by Jacobs and Simpson (*J. Biol. Chem.*, 1935, **110**, 565). A quinoxaline could not be obtained by the action of *o*-phenylenediamine, but the addition of 4 : 5-diaminouracil sulphate to an alcoholic solution of the ester gave a yellow solution with a strong green fluorescence.

The extract B was acidified and extracted with ether and a solid was obtained on evaporation of the extract, forming long slender needles, m. p. 220° after two crystallisations from alcohol; it appeared to be a fairly acidic *lactone* (Found: C, 71·9; H, 9·3. $C_{20}H_{30}O_4$ requires C, 71·8; H, 9·1%).

Action of Hydrogen Bromide on the Acetoxy-lactone.—1·5 G. of the lactone, dissolved in 60 c.c. of alcohol, were kept ice-cold and saturated with dry hydrogen bromide (4 hours). The product was liberated by pouring into water, and taken up in ether, the extract being washed with water, sodium bicarbonate, dried and evaporated, a red-brown gum being obtained. As this did not solidify, a 4% solution of it in benzene was allowed to percolate through a column of activated alumina. A much lighter-coloured product (800 mg.) was recovered on evaporation, and 200 mg. of colourless crystals were obtained on elution of the alumina with ether and evaporation of the ether. The crystals were readily soluble in the usual organic solvents except benzene, from which they separated in needles, m. p. 201°. These were free from halogen and saturated to bromine and permanganate, but developed a yellow colour with tetranitromethane in chloroform, and dissolved in alkali, being reprecipitated by acids; the compound was thus a *lactone* differing from the original acetoxy-lactone by one molecule of water (Found: C, 77·8; H, 9·3. $C_{24}H_{34}O_3$ requires C, 77·8; H, 9·3%).

The bromine-containing gum (800 mg.) in boiling acetic acid was treated with small quantities of zinc dust in the course of 5 hours. Water was then added, and the product taken up in ether, the extract freed from acid with bicarbonate, dried, and evaporated. The residue solidified on rubbing with methyl alcohol, and was recrystallised from this solvent, then twice from ethyl alcohol, forming microscopic needles, m. p. 99°. It was a *lactone* and apparently saturated (Found: C, 80·2; H, 10·0. $C_{22}H_{32}O_2$ requires C, 80·4; H, 9·9%).

Hydroxy-lactone (III).—The acetoxy-lactone (1·27 g.) in 105 c.c. of alcohol was boiled for 50 minutes with 280 c.c. of 5% alcoholic potassium hydroxide, the solution then poured into water and extracted with ether. The aqueous layer was acidified with 10% sulphuric acid and re-extracted with ether, the extract washed, dried, and evaporated, yielding 900 mg. of *hydroxy-lactone*, long needles, m.p. 202° after two crystallisations from alcohol [a better solvent is acetone–petroleum (b. p. 60—80°)] (Found: C, 75·9; H, 9·5. $C_{22}H_{34}O_3$ requires C, 76·2; H, 9·5%). It had $[\alpha]_D^{25°}$ − 36·2, $[\alpha]_{5461}^{25°}$ − 44·2, $[\alpha]_D/[\alpha]_{5461}$ 1·22 (c = 0·733 in chloroform); Dr. R. K. Callow informs us that the compound showed no progestin-like activity when tested on a rabbit.

Keto-lactone (IV).—900 Mg. of the hydroxy-lactone (III) in 65 c.c. of acetic acid were treated dropwise and with constant shaking with 720 mg. of chromic acid in 9 c.c. of acetic acid in the

* We are again indebted to Dr. R. K. Callow for determining the rotations recorded in this work.

course of 30 minutes. The solution was kept for 2½ hours, poured into water, and repeatedly extracted with a large volume of ether. The extract was shaken three times with water, then with 5% sodium carbonate solution, again with water, dried, and evaporated; 730 mg. of the *keto-lactone* were obtained, forming short glassy needles, m. p. 184·5° after one crystallisation from rectified spirit (the m. p. is depressed 30° by the acetoxy-lactone) (Found: C, 76·7, 76·4; H, 9·0, 9·3. $C_{22}H_{32}O_3$ requires C, 76·7; H, 9·4%).

Deoxy-lactone.—380 Mg. of the above lactone in 69 c.c. of alcohol were boiled for 7½ hours with a large excess of amalgamated zinc, whilst 13 c.c. of hydrochloric acid were added in small portions during that time. The solution was poured into water and extracted with ether, the extract being well washed, dried, and evaporated. The residue was a light brown oil (370 mg.) which solidified on rubbing with methyl alcohol. After one crystallisation from this solvent it formed flattened needles, m. p. 133·5°, but after melting and resolidification it melted at 128°, the figure given by Jacobs and Simpson (*loc. cit.*) for the compound prepared from deoxysarsasapogenin (Found: C, 79·9; H, 10·2. Calc.: C, 79·9; H, 10·4%).

Degradation of the Deoxy-lactone.—A solution of 9·2 g. of the deoxy-lactone in 450 c.c. of ether was run dropwise (30 mins.) into a mechanically stirred solution of Grignard reagent prepared from 36 g. of bromobenzene, 4·95 g. of magnesium, and 135 c.c. of ether. The solution was boiled under reflux for 6 hours, the ether then distilled off, and the dark residue treated with ice and dilute sulphuric acid. The product was taken up in ether, the extract washed, dried, and evaporated, yielding a brown syrup which partly solidified on keeping. It was warmed with 100 c.c. of acetic acid, an almost colourless solid being deposited (8·7 g.); this was insoluble in acetic acid and practically so in methyl alcohol, but freely soluble in benzene. After two crystallisations from methyl alcohol–acetone, it formed glistening needles, m. p. 205·5°, evidently containing acetone of crystallisation (Found: in air-dry material, C, 81·2; H, 10·0; after drying at 130° in a high vacuum, C, 83·5; H, 9·3. $C_{34}H_{46}O_2,C_3H_6O$ requires C, 81·6; H, 9·6%. $C_{34}H_{46}O_2$ requires C, 83·9; H, 9·5%); it was therefore the *diphenylcarbinol* (V).

8·6 G. of the crude carbinol were suspended in 215 c.c. of acetic acid in a three-necked flask (see p. 417), and heated on a steam-bath. 12·9 G. of chromic acid in 30 c.c. of 80% acetic acid were dropped in during 30 minutes, and the stirring continued for a further 3 hours. The solution was diluted with 750 c.c. of water made just acid with sulphuric acid, repeatedly extracted with much ether, and the extract washed free from acetic acid with the same slightly acid water, and finally with distilled water; emulsions tended to form at first. The extract was now shaken three times with 2*N*-sodium hydroxide; a dark brown, viscous sodium salt separated between the two layers. The clear alkaline solution was acidified with sulphuric acid, and the acid isolated by means of ether as a yellow-brown oil. This was taken up in a little warm acetic acid, and water was added until a slight turbidity appeared. After some time, the solution deposited crude ætiobilianic acid (180 mg.); this was recrystallised four times from dilute acetic acid (charcoal) and formed dense prisms, m. p. 226·5°. A sample of the acid kindly sent by Prof. H. Wieland melted at 225·5° and a mixture of the two had an intermediate m. p. (Found: C, 70·9; H, 9·7. Calc. for $C_{19}H_{34}O_4$: C, 70·8; H, 9·4%). A small amount was sublimed in a vacuum, giving the anhydride, m. p. 203° (Wieland, Schlichting, and Jacobi, *Z. physiol. Chem.*, 1926, **161**, 80, give m. p. 206°).

The viscous sodium salt obtained as a by-product gave on acidification a gummy acid, which was isolated by means of ether (450 mg.); it solidified after some months and crystallised from dilute alcohol in needles, m. p. 212—213°. It was probably the *acid* (VI) analogous to the product obtained by Tschesche and Hagedorn (*Ber.*, 1935, **68**, 1412) from tigogenin (Found: C, 78·8; H, 8·8. $C_{37}H_{42}O_4$ requires C, 79·3; H, 8·2%).

Oxidation of Smilagenin Acetate.—This was carried out exactly as described on p. 417, 1·5 g. of acetoxy-lactone being obtained from 9·2 g. of smilagenin acetate. The compound melted at 184·5° after one crystallisation from alcohol, and did not depress the m. p. of the corresponding compound from sarsasapogenin; it had $[\alpha]_D^{25°} - 32·0$, $[\alpha]_{5461}^{25°} - 37·8$, $[\alpha]_D/[\alpha]_{5461} = 1·18$ ($c = 0·972$ in chloroform) (these values are regarded as more accurate than those given on p. 417) (Found: C, 74·4, 74·3; H, 9·3, 9·4. Calc. for $C_{24}H_{36}O_4$: C, 74·2; H, 9·3%).

3-Methylcholestan-3-ol.—β-Cholestanone was obtained by the method of Vavon and Jakubowicz (*Bull. Soc. Chim. biol.*, 1933, **53**, 581) as modified by Callow (private communication). 194 G. of the ketone in 2 l. of ether were added in a rapid stream to a Grignard reagent prepared from 336 g. of methyl iodide, 47·8 g. of magnesium activated by heating with iodine, and 1 l. of ether. The solution, which did not deposit a solid addition compound, was boiled under reflux for 2 hours, the solvent distilled off, the grey semi-solid residue decomposed with ice and dilute sulphuric acid, and the product taken up in ether. The extract was washed with caustic soda,

water, dried, and evaporated, the residue being crystallised from acetic acid, giving plates, m. p. about 97° (195 g.); these were rather soluble in the usual organic solvents and evidently consisted of a mixture of two isomerides. One of these was obtained pure after repeated crystallisation from acetic acid and had the constant m. p. 147° (Found: C, 84·2; H, 12·5. $C_{28}H_{50}O$ requires C, 83·9; H, 12·1%).

3-*Methyl*-$\Delta^{3(?)}$-*cholestene*.—An attempt to dehydrate the above carbinol with thionyl chloride in pyridine (Darzens, *Compt. rend.*, 1911, **152**, 601) was unsuccessful; the product, obtained in poor yield, formed clusters of needles, m. p. 98°, from alcohol, and contained halogen. The carbinol could be distilled unchanged in a high vacuum, but when distilled in the presence of a little aniline hydrobromide it lost water; the distillate was unsaturated to bromine and tetranitromethane and crystallised from acetone in fine prisms, m. p. 81—82° (Found: C, 87·6; H, 12·4. $C_{28}H_{48}$ requires C, 87·8; H, 12·2%).

Dehydrogenation of 3-*Methylcholestan*-3-*ol*.—50 G. of the carbinol were heated with 75 g. of selenium in a stream of nitrogen, a bath of sodium and potassium nitrates being used to maintain a constant temperature. In the first experiment a certain amount of frothing was experienced, possibly due to incomplete removal of solvents, and the temperature of the bath was raised gradually; it was kept at 270° for 3 hours, at 310—320° for 15 hours, and at 340° for 3 hours. The products were then extracted with ether, and the filtered solution evaporated, the residue being distilled at 1·2 mm. A few drops boiled below 200°, 5·7 g. at 200—225° (this contained much selenium), and 35 g. of a yellow, slightly fluorescent oil were collected at 225—235° (mainly 229—231°). This solidified almost completely overnight, and was purified by rubbing with acetone and successive recrystallisation from acetone, alcohol, and acetone, flattened needles, m. p. 96—97°, being obtained; they were evidently 3-*methylcholestane* (Found: C, 86·9; H, 13·2. $C_{28}H_{50}$ requires C, 86·9; H, 13·1%).

The compound was again subjected to dehydrogenation for 46 hours at 350—360°. After extraction with ether and evaporation of the solvent, a thick dark oil with a green fluorescence was obtained; it was dissolved in petroleum (b. p. 60—80°), filtered from some insoluble material, and the solution (approximately 1%) allowed to percolate through a 30-cm. column of Merck's activated alumina (compare Gamble, Kon, and Saunders, J., 1935, 644); this was followed by an equal volume of the pure solvent. The yellow oil recovered on evaporation was treated with *s*-trinitrobenzene, a brownish-orange compound being formed. This melted at about 150° after two crystallisations from alcohol; the hydrocarbon regenerated from it by means of stannous chloride was not homogeneous, as the m. p. altered with every crystallisation; a preparation melting at about 165° gave analytical figures corresponding to a *dimethyl*cyclo*pentenophenanthrene* (Found: C, 92·6; H, 7·4. $C_{19}H_{18}$ requires C, 92·6; H, 7·4%).

In another experiment the carbinol was carefully dried, and the temperature of the bath maintained at 330—340° for 16 hours and at 355—360° for a further 24 hours. The dehydrogenation proceeded smoothly. The products were extracted as before, and purified with alumina without previous distillation, 18 g. of reddish oil being recovered. This was treated with 12 g. of *s*-trinitrobenzene dissolved in benzene and a little alcohol. 9·5 G. of crude complex separated overnight, and a further 10 g. were obtained on concentrating the mother-liquor and rubbing the resulting red oil with petroleum (b. p. 40—60°). The total solid was purified by rubbing with this solvent, and the hydrocarbon was regenerated from it by dissolving in alcohol (750 c.c.) and adding a hot solution of 50 g. of stannous chloride in a little hydrochloric acid. After boiling for a short time, the alcohol was removed under reduced pressure, and the hydrocarbon recovered by adding water and extraction with ether; persistent emulsions were formed. The hydrocarbon was purified once more by the alumina process, and was recovered in two portions, 2·3 g. (*A*) representing the more soluble, less easily adsorbed and nearly colourless solid, and 2·6 g. (*B*), which was pale yellow and was recovered from the later runnings; *A* was almost completely soluble in alcohol, and crystallised in iridescent plates (1·1 g.), m. p. 90—100 (*A'*), and the mother-liquor on concentration gave an oil. The latter was reconverted into the trinitrobenzene compound, and this recrystallised from alcohol, but a compound of definite m. p. could not be obtained in this way (see below), and the same applies to the complex prepared from *A'*. Similarly, *B* was crystallised from alcohol, but a compound of definite m. p. was not obtained from it, the m. p. rising gradually to over 210°; this gave a trinitrobenzene complex, m. p. about 165° after one crystallisation.

As the result of the experience on the dehydrogenation of methylsarsasapogenin (p. 420), *cyclo*hexane was employed for the crystallisation of the *trinitrobenzene complex*; in this way fine silky needles, m. p. 174—175°, were obtained after a long series of crystallisations; these were apparently derived from a methyl*cyclo*pentenophenanthrene (Found: C, 64·6, 64·6, 64·5; H, 4·1,

4·1, 4·0. $C_{24}H_{19}O_6N_3$ requires C, 64·7; H, 4·3%). The hydrocarbon regenerated from it was purified by the alumina method, but it was not homogeneous, as the least soluble fraction obtained in minute amount by crystallisation from alcohol melted at about 165°, whilst the bulk formed flattened needles melting at about 120°; a hydrocarbon of constant m. p. has not yet been obtained. The portions of low m. p. gave a *picrate*, orange-red needles from alcohol, m. p. 145—146° (Found: C, 62·3; H, 4·45. $C_{24}H_{19}O_7N_3$ requires C, 62·5; H, 4·2%), a *s*-trinitrobenzene *compound*, yellow needles from alcohol, m. p. 181—182° (Found: C, 64·3; H, 4·1%), and a *styphnate*, aggregates of yellow needles from alcohol, m. p. 175—176° (Found: C, 60·8; H, 4·45. $C_{24}H_{19}O_8N_3$ requires C, 60·4; H, 4·0%). It is noteworthy that these derivatives are all stable to hot alcohol.

3-*Methylsarsasapogenin*.—5 G. of sarsasapogenone (Jacobs and Simpson, *J. Biol. Chem.*, 1935, **109**, 501) in 400 c.c. of ether were added to a Grignard reagent prepared from 15·6 g. of methyl iodide as described on p. 418. The crude *carbinol* was obtained in almost quantitative yield and had m. p. 185° (not depressed by the addition of the parent ketone); it was clearly homogeneous, as the m. p. remained constant after crystallisation from *cyclo*hexane and from acetone; it formed flattened needles (Found: C, 78·1, 78·2; H, 10·8, 10·8. $C_{28}H_{46}O_3$ requires C, 78·1; H, 10·8%).

Dehydrogenation. 86 G. of the carbinol were dehydrogenated with 130 g. of selenium at a bath temperature of 350° for 33 hours, and the product worked up as described on p. 419. The greater part of this was insoluble in petroleum, and was a dark brown gum which gradually solidified and is still under investigation. After the first treatment with alumina, 8·5 g. of an amber oil (*A*) and 3·8 g. of a yellow solid (*B*) were obtained, corresponding roughly to *A* and *B* above. These were separately treated with *s*-trinitrobenzene, but the solid obtained in each case contained much of the reagent, from which it had to be separated by repeated extraction with *cyclo*hexane and could then be recovered by evaporation of the extract. As a compound of constant m. p. could not be obtained by crystallisation from alcohol, the crude complex was once recrystallised from this solvent, and the hydrocarbon regenerated from it and fractionally crystallised from alcohol; the m. p. of this rose steadily until it reached 215—216°, but the process could not be continued owing to lack of material. The *hydrocarbon* formed iridescent plates corresponding in composition to the formula $C_{19}H_{16}$ (Found: C, 93·4; H, 6·6. $C_{19}H_{16}$ requires C, 93·4; H, 6·6%). The hydrocarbon was dissolved in alcohol (it was very sparingly soluble) and a little benzene and treated with *s*-trinitrobenzene. The orange solution did not deposit the complex until it had been concentrated, whereupon a deep brownish-orange complex, m. p. 157—158°, was obtained. On dissolving this in alcohol and cooling, the hydrocarbon separated out, but the complex was re-formed on adding more trinitrobenzene; it now had m. p. 164—166°, not depressed by admixture of the complex of similar m. p. from methylcholestanol. It is evident that this complex decomposes very readily in alcoholic solution, and this may account for the difficulties experienced when this solvent is employed for the crystallisation of mixtures. From the more soluble portions of the hydrocarbon mixture, a *s*-trinitrobenzene complex was prepared and crystallised from *cyclo*hexane, orange needles, m. p. 174—175°, being obtained; these were in every way identical with the complex described on p. 419 (mixed m. p.) (Found: C, 64·7, 64·6, 64·8; H, 4·1, 4·3, 4·2. Calc.: C, 64·7; H, 4·3%).

From a portion of the trinitrobenzene complex which could not be crystallised to a constant m. p., a hydrocarbon mixture was obtained; after repeated crystallisation from alcohol, a material melting rather indefinitely at about 220° was produced, giving a *s*-trinitrobenzene *complex*, m. p. 161—163° after one crystallisation from *cyclo*hexane. It formed dark orange needles, and its m. p. was depressed by admixture of the foregoing compound (Found: C, 60·3; H, 3·7. $C_{19}H_{13}O_6N_3$ requires C, 60·3; H, 3·5%); it could not be further examined owing to lack of material.

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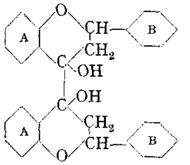
90. *The Constitution of Tannins. Part V. The Synthesis of some Flavpinacols.*

By ALFRED RUSSELL and JOHN TODD.

IN previous communications (J., 1934, 218, 1066, 1506, 1940) several polyhydroxy-derivatives of flavpinacol (I), in which B consisted of a catechol residue and A was built up from a resorcinol, phloroglucinol, or pyrogallol nucleus, were shown to be qualitatively indistinguishable from typical natural phlobatannins and to be capable, in aqueous solution, of tanning sheepskin. The series of synthetic flavpinacols has been extended with a view to the determination of the simplest structure of the flavpinacol type to exhibit the properties of a tannin, and we now describe corresponding series of flavpinacols in which B has been derived from (*a*) vanillin and (*b*) *p*-hydroxybenzaldehyde. Without exception, the products in each of these series are insoluble in water and therefore not directly comparable with natural phlobatannins.



(I.)

On the other hand, the flavpinacol obtained by the reduction of 2 : 3′ : 4′-trihydroxychalkone, *i.e.*, the flavpinacol containing *o*-hydroxyl groups in the 3′ : 4′-positions in residue B but without hydroxyl groups in residue A, is soluble in water and was shown by qualitative reactions to be related to natural phlobatannins. An aqueous solution of this preparation transformed a piece of sheepskin into a leather-like mass which showed no sign of decomposition after exposure for several months. Thus the presence of two hydroxyl groups in residue B, provided they are situated at the 3′ : 4′-positions, is sufficient to enable the flavpinacol to show tanning properties. We are now seeking to determine whether this condition is essential or not.

The number and disposition of hydroxyl groups in residue B influence the solubility of a flavpinacol in water to a much greater extent than similar groups in residue A. The number and orientation of such groups in residue A, on the other hand, have the greater effect on the colour: an increase in the number intensifies it and the effect is greatest when the groups are vicinal to each other.

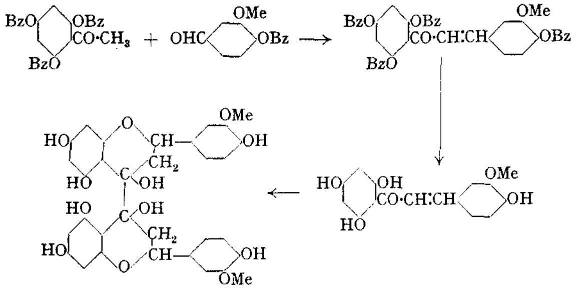
The views of Asahina, Shinoda, and Inubuse (*Chem. Abs.*, 1928, **22**, 2946) on the constitutions of eriodictyol (fawn-coloured leaflets, m. p. 267°) and homoeriodictyol (pale yellow plates, m. p. 223°) have been confirmed. Power and Tutin, who isolated these substances from the leaves of *Eriodictyon californicum* and of *E. glutinosum*, considered them to be, respectively, 2 : 4 : 6 : 3′ : 4′-pentahydroxychalkone and its 3′-monomethyl ether (J., 1907, **91**, 887). The Japanese workers formulated them as the corresponding flavanones. Chalkones of the above constitutions have now been obtained by an unambiguous route; they crystallise from dilute alcohol, the former in orange-brown microscopic prisms, m. p. 245°, and the monomethyl ether in orange prisms, m. p. 214°. Each, when recrystallised from 70% acetic acid, is converted into the corresponding flavanone, 5 : 7 : 3′ : 4′-tetrahydroxyflavanone, fawn-coloured lustrous plates, m. p. 267°, evidently identical with eriodictyol, and 5 : 7 : 4′-trihydroxy-3′-methoyxflavanone, fawn-coloured plates, m. p. 219—220°, the homoeriodictyol of Power and Tutin.

The required chalkones were synthesised by condensation of appropriate benzoylated derivatives of *o*-hydroxyacetophenone and of benzaldehyde in ethyl acetate solution at 0° in the presence of anhydrous hydrogen chloride, the resulting benzoylated chalkone being hydrolysed with alkali in an atmosphere of nitrogen. Where possible, the benzoic acid was separated from the hydroxychalkone with boiling benzene. The solubility of the chalkones in benzene, however, increases as the number of hydroxyl groups decreases; so, in cases where the solubility of the chalkone in this solvent was appreciable, the separation from benzoic acid was accomplished with dilute sodium carbonate solution in an atmosphere of carbon dioxide.

The lower hydroxychalkones were reduced with zinc dust and acetic acid, but in the reduction of the more highly hydroxylated chalkones zinc dust and alcoholic hydrogen

chloride were used, since the acidity of the hydroxychalkones increased with the number of hydroxyl groups.

The following scheme, which is typical for the series, shows the synthesis of 2 : 4 : 6 : 4'-tetrahydroxy-3'-methoxychalkone and its reduction to *bis*-(5 : 7 : 4'-*trihydroxy*-3'-*methoxy*)-*flavpinacol* :



EXPERIMENTAL.

2 : 4'-*Dibenzoyloxy*-3'-*methoxychalkone*.—The colourless solution of *o*-benzoyloxyacetophenone (9·6 g.) and vanillin benzoate (10·3 g.; slight excess over 1 mol.) in dry ethyl acetate (100 c.c.), saturated at 0° with anhydrous hydrogen chloride, protected from moisture, and kept in ice for 24 hours, became yellow, orange, orange-red, and finally clear red. Dry air was then drawn through it during 2 hours, the solvent distilled off on the water-bath, and the residual reddish syrup taken up in boiling alcohol (*ca.* 100 c.c.). The cooled solution was decanted from the precipitated, pale yellow, semi-solid mass, which was washed twice with cold alcohol and used in the hydrolysis to the hydroxychalkone. A specimen crystallised from alcohol formed topaz-coloured prisms with pointed ends, m. p. 118—119° (Found : C, 75·5; H, 4·3. $C_{30}H_{22}O_6$ requires C, 75·3; H, 4·6%).

2 : 4'-*Dihydroxy*-3'-*methoxychalkone*.—The crude benzoate (13·5 g.), dissolved in alcohol (*ca.* 100 c.c.), was boiled with 4% aqueous caustic potash (200 c.c.; 5 mols.) in an atmosphere of nitrogen for 4 hours, the alcohol then having distilled off. The cooled solution was acidified and saturated with sodium chloride, the pale yellow precipitate collected and shaken with dilute aqueous sodium carbonate (carbon dioxide atmos.), and the *chalkone* filtered rapidly, washed with water, and recrystallised from dilute alcohol (charcoal), forming pale orange-coloured needles, m. p. 128° (Found : C, 71·1; H, 5·1. $C_{16}H_{14}O_4$ requires C, 71·1; H, 5·2%).

Bis-(4'-*hydroxy*-3'-*methoxy*)*flavpinacol*.—To a boiling solution of 2 : 4'-dihydroxy-3'-methoxychalkone (2 g.) in alcohol (30 c.c.), alcoholic hydrogen chloride (15 c.c., saturated at 0°) was added, followed by zinc dust (5 g.). After 10 minutes' boiling, the solution, now colourless, was filtered hot, cooled rapidly, diluted with water, and extracted with ethyl acetate. The extract was washed with water until free from halogen, dried (sodium sulphate), and evaporated under diminished pressure. The *product* was a light red, amorphous powder, insoluble in water and in acids, soluble in alkalis and in the common organic solvents (Found : C, 71·2; H, 5·4. $C_{32}H_{30}O_8$ requires C, 70·8; H, 5·5%).

2 : 4 : 4'-*Trihydroxy*-3'-*methoxychalkone*.—Resacetophenone dibenzoate (7·2 g.) and vanillin benzoate (5·5 g.), condensed in the above-described manner, gave 2 : 4 : 4'-*tribenzoyloxy*-3'-*methoxychalkone* (12 g. approx.), which separated from alcohol in pale yellow, amorphous nodules, m. p. 148° (sintering 131°) (Found : C, 73·3; H, 4·5. $C_{36}H_{26}O_8$ requires C, 74·3; H, 4·35%). The benzoate was hydrolysed as before (nitrogen atmos.) and the pale yellow solid obtained after acidification of the reaction mixture was collected, dried, and extracted (Soxhlet), first with benzene to remove the benzoic acid and then with acetone. The acetone was removed on the water-bath, and the residue recrystallised from dilute alcohol, forming canary-yellow microscopic prisms, m. p. 210°. For analysis the substance was dried

over caustic soda for 2 hours at 120°/15 mm. (Found: C, 66·8; H, 5·0. $C_{18}H_{14}O_5$ requires C, 67·1; H, 4·9%).

Bis-(7 : 4'-dihydroxy-3'-methoxy)flavpinacol was obtained by reduction of the preceding chalkone, as a deep red, amorphous solid, insoluble in water and in acids, soluble in alkalis to dark red solutions and in the usual organic solvents (Found in material dried over sodium hydroxide for 8 hours at 120°/15 mm.: C, 67·5; H, 5·4. $C_{32}H_{30}O_{10}$ requires C, 67·0; H, 5·2%).

2 : 4 : 6 : 4'-*Tetrahydroxy-3'-methoxychalkone*.—The *tetrabenzoate*, prepared by condensation of phloracetophenone tribenzoate (9·6 g.) and vanillin benzoate (5·5 g.), formed pale yellow, non-crystalline nodules (14 g. approx.) (Found in substance dried for 5 hours over sodium hydroxide at 80°/15 mm.: C, 73·8; H, 4·1. $C_{44}H_{30}O_{10}$ requires C, 73·5; H, 4·2%). The chalkone resulting from its hydrolysis in a nitrogen atmosphere was purified by the benzene extraction method and recrystallised from dilute alcohol; it formed deep orange-coloured, microscopic prisms, m. p. 214° (slight sintering at 210°) (cf. Mossler, *Annalen*, 1907, **351**, 243).

A mustard-yellow salt of the chalkone was obtained when carbon dioxide was passed into the alkaline solution after hydrolysis of the benzoate. The salt, on recrystallisation from 70% acetic acid, yielded the flavanone, homoeriodictyol.

Bis-(5 : 7 : 4'-trihydroxy-3'-methoxy)flavpinacol.—Acetic acid (10 c.c.) and zinc dust (5 g.) were added to a boiling solution of 2 : 4 : 6 : 4'-tetrahydroxy-3'-methoxychalkone (2 g.) in alcohol (10 c.c.). After boiling for 10 minutes, the hot solution was filtered, cooled, diluted with water, almost neutralised with aqueous bicarbonate, saturated with sodium chloride, and extracted with ethyl acetate. The clear red extract was dried (sodium sulphate) and evaporated to dryness under diminished pressure. The residue was dissolved in acetone, treated with charcoal, filtered, and the acetone removed under reduced pressure. The residual vitreous mass yielded, on grinding, a light red amorphous powder, soluble in alkalis to deep red solutions, insoluble in acids, sparingly soluble in hot water, and readily soluble in the usual organic solvents. For analysis, it was dried over sodium hydroxide for 2 hours at 120°/15 mm. (Found: C, 64·3; H, 4·8. $C_{32}H_{30}O_{12}$ requires C, 63·5; H, 4·95%).

2 : 3 : 4 : 4'-*Tetrahydroxy-3'-methoxychalkone*.—Condensation of gallacetophenone tribenzoate (9·6 g.) and vanillin benzoate (5·5 g.) gave in the normal manner 2 : 3 : 4 : 4'-*tetrabenzoyloxy-3'-methoxychalkone* (approx. 14 g.) as a pale orange-yellow, friable solid, m. p. 95° after softening (Found: C, 72·5; H, 4·7. $C_{44}H_{30}O_{10}$ requires C, 73·5; H, 4·2%. $C_{44}H_{30}O_{10},C_2H_6O$ requires C, 72·4; H, 4·7%). The *hydroxychalkone* was obtained by hydrolysis of the above benzoate (nitrogen atmosphere), separated from benzoic acid by means of dilute sodium carbonate solution, and recrystallised from dilute aqueous alcohol, forming orange-brown prisms, m. p. 199—200° (Found: C, 64·2; H, 4·7. $C_{16}H_{14}O_6$ requires C, 63·6; H, 4·6%).

Bis-(7 : 8 : 4'-trihydroxy-3'-methoxy)flavpinacol was obtained, by reduction of the preceding chalkone with zinc dust and alcoholic hydrogen chloride, as a dark brown, amorphous powder, soluble in alkali to a very dark opaque solution, insoluble in acids, very sparingly soluble in hot water, and readily soluble in the common organic solvents (Found in substance dried for 6 hours over sodium hydroxide at 120°/15 mm.: C, 64·0; H, 5·1. $C_{32}H_{30}O_{12}$ requires C, 63·5; H, 4·95%).

2 : 4'-*Dihydroxychalkone*.—Condensation of *o*-benzoyloxyacetophenone (9·6 g.) and *p*-benzoyloxybenzaldehyde (9·1 g.) in dry ethyl acetate (*ca.* 100 c.c.) with anhydrous hydrogen chloride gave a pale orange, semi-solid mass. A dilute alcoholic solution of this *dibenzoate* slowly deposited pale yellow prisms, m. p. 120° (Found: C, 78·1; H, 4·2. $C_{29}H_{20}O_5$ requires C, 77·7; H, 4·46%). Hydrolysis with alcoholic caustic potash (nitrogen atmos.) and extraction of the product with dilute sodium carbonate solution (carbon dioxide atmos.) left the *chalkone*, which crystallised from dilute alcohol in pale yellow needles, m. p. 145° (Found in substance dried over sodium hydroxide in a vacuum desiccator: C, 75·4; H, 5·0. $C_{15}H_{12}O_3$ requires C, 75·0; H, 5·0%).

Bis-(4'-hydroxy)flavpinacol.—2 : 4'-Dihydroxychalkone (2 g.) was reduced with zinc dust (5 g.) and alcoholic hydrogen chloride (50 c.c.). The product (1·5 g.) was an orange-red friable solid, soluble in alkalis to clear red solutions, insoluble in acid and in water, readily soluble in alcohol and ether (Found: C, 75·0; H, 5·3. $C_{30}H_{26}O_6$ requires C, 74·7; H, 5·4%).

2 : 4 : 4'-*Trihydroxychalkone*.—Resacetophenone dibenzoate (7·2 g.) and *p*-benzoyloxybenzaldehyde (4·7 g.) gave in the usual manner 2 : 4 : 4'-*tribenzoyloxychalkone*, which formed pale yellow prisms, m. p. 114—115°, from alcohol (Found for substance kept over potassium hydroxide in a vacuum desiccator for 9 days: C, 75·2; H, 4·55. $C_{36}H_{24}O_7$ requires C, 76·1; H, 4·23%. $C_{36}H_{24}O_7,C_2H_6O$ requires C, 74·5; H, 4·9%).

2 : 4 : 4'-*Trihydroxychalkone*, obtained by hydrolysis of the above product by means of alco-

holic caustic potash (nitrogen atmos.) and separation of the benzoic acid with dilute aqueous sodium carbonate solution (carbon dioxide atmos.), formed pale yellow needles, m. p. 187—188°, from dilute alcohol (Found: C, 70·1; H, 4·6. $C_{15}H_{12}O_4$ requires C, 70·3; H, 4·7%).

Bis-(7 : 4'-dihydroxy)flavpinacol was prepared by reduction (zinc dust–acetic acid) of an alcoholic solution of 2 : 4 : 4'-trihydroxychalkone and isolated as a deep orange-red, amorphous powder, insoluble in water and in acids, soluble in alkalis and in alcohol and ether. The substance for analysis was dried over sodium hydroxide at 120°/15 mm. for 5 hours (Found: C, 70·0; H, 5·05. $C_{30}H_{26}O_8$ requires C, 70·0; H, 5·05%).

2 : 3 : 4 : 4'-*Tetrahydroxychalkone*.—2 : 3 : 4 : 4'-*Tetrabenzoyloxychalkone* was obtained by condensation of gallacetophenone tribenzoate (9·6 g.) and *p*-benzoyloxybenzaldehyde (4·7 g.) and isolated in pale yellow, non-crystalline nodules, m. p. 105° after softening (Found: C, 74·0; H, 4·1. $C_{43}H_{28}O_9$ requires C, 74·9; H, 4·1%). 2 : 3 : 4 : 4'-*Tetrahydroxychalkone*, prepared by hydrolysis (alcoholic potassium hydroxide; nitrogen atmos.) of the above benzoate (benzoic acid removed by benzene extraction), crystallised from dilute aqueous alcohol in reddish-brown needles, m. p. 117° (Found: C, 65·8; H, 4·5. $C_{15}H_{12}O_5$ requires C, 66·2; H, 4·4%).

Bis-(7 : 8 : 4'-trihydroxy)flavpinacol was obtained, by reduction of the chalkone with zinc dust and alcoholic hydrogen chloride, as a deep brown, amorphous solid, sparingly soluble in hot water, insoluble in acids, soluble in alkalis to dark brown solutions and in alcohol, acetone, and ether (Found for substance dried over sodium hydroxide for 1½ hours at 120°/15 mm.: C, 66·0; H, 4·95. $C_{30}H_{26}O_{10}$ requires C, 65·9; H, 4·80%).

2 : 4 : 6 : 4'-*Tetrahydroxychalkone*.—Phloracetophenone tribenzoate (9·6 g.) and *p*-benzoyloxybenzaldehyde (4·7 g.) were condensed in the usual manner. The resulting 2 : 4 : 6 : 4'-*tetrabenzoyloxychalkone* was obtained in pale yellow nodules (12 g.) (Found: C, 74·6; H, 3·9. $C_{43}H_{28}O_9$ requires C, 74·9; H, 4·1%). Hydrolysis yielded 2 : 4 : 6 : 4'-*tetrahydroxychalkone*, which was separated from benzoic acid by benzene extraction and recrystallised from dilute alcohol, forming microscopic orange prisms, m. p. 205°. It was dried for 2 hours over sodium hydroxide at 120°/15 mm. (Found: C, 66·1; H, 4·5. $C_{15}H_{12}O_5$ requires C, 66·2; H, 4·4%).

Bis-(5 : 7 : 4'-trihydroxy)flavpinacol was obtained from the chalkone, by reduction with zinc dust and alcoholic hydrogen chloride, as an orange-brown, amorphous solid, soluble in alkalis to dark red solutions, insoluble in acids and in water, readily soluble in alcohol and in ether. A specimen was dried over sodium hydroxide for 2 hours at 120°/15 mm. (Found: C, 66·7; H, 4·9. $C_{30}H_{26}O_{10}$ requires C, 66·0; H, 4·8%).

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THE UNIVERSITY, GLASGOW. [Received, December 28th, 1936.]

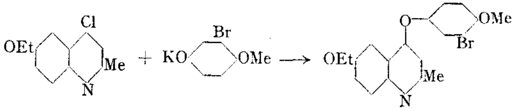
91. *Aryloxy-derivatives of Pyrimidines, Quinoxalines, and Quinolines.*

By DIANA LOCKHART and E. E. TURNER.

IT is frequently assumed that one of the important constitutional factors conferring antimalarial activity on quinine and its analogues is the presence of two discrete basic centres in the molecule. We have prepared, for examination by the Chemotherapy Committee of the Medical Research Council, a number of aryloxy-compounds. The readily accessible 2 : 4 : 6-trichloropyrimidine has been found to react smoothly with potassium phenoxides, and in this way 2 : 4 : 6-*triphenoxy-*, 2 : 4 : 6-*tri*-p-*anisoxy-*, 2 : 4 : 6-*tri*-p-*tolyloxy-* and 2 : 4 : 6-*tri*-p-*chlorophenoxy-pyrimidine* have been obtained. Similar replacement of reactive halogen was effected in the quinoxaline series, and from 2 : 3-dichloroquinoxaline four 2 : 3-diaryloxyquinoxalines have been made. In addition, 2 : 3-*dianilino-*, 2 : 3-*di*-m-*toluidino-* and 2 : 3-*di*-p-*toluidino-quinoxaline* have been prepared.

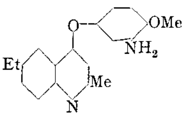
In the quinoline series, the starting material chosen was 4-*chloro-6-ethoxy-2-methylquinoline*, which is readily obtainable from the corresponding, known, 4-hydroxy-compound. The chlorine atom was found to react with potassium phenoxides, and has been successfully replaced by the phenoxy-, *p*-tolyloxy-, *p*-anisoxy-, and *p*-chlorophenoxy-groups. The anisoxy-compound seemed to be of greatest interest, since mononitration, followed by reduction, should lead to 4-m-*amino*-p-*methoxyphenoxy-6-ethoxy-2-methyl-*

quinoline (II), a substance possessing not only the right kind of disposition of basic centres but also the alkoxy-groups. The above nitration did actually take place in the sense mentioned, for replacement of the amino-group in (II) gave a *bromo*-compound (I), identical with that obtained by condensing potassium 3-bromo-4-methoxyphenoxide with 4-chloro-6-ethoxy-2-methylquinoline :

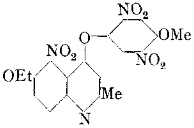


(I.)

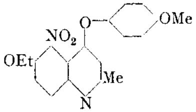
Further nitration of the mononitro-compound or of the parent anisoxy-compound could not be caused to stop when only one more nitro-group had been introduced, but the trinitro-compound, which we regard as (III), was readily obtained.



(II.)



(III.)



(IV.)

4-Chloro-6-ethoxy-2-methylquinoline is nitrated to give a compound which, by well-established analogies, must be 4-*chloro*-5-*nitro*-6-*ethoxy*-2-*methylquinoline*, and the latter reacts with potassium *p*-methoxyphenoxide to give (IV). This compound resembled its isomeride in that it refused to undergo simple mononitration.

Experimental.

2 : 4 : 6-*Triphenoxypyrimidine*.—Potassium hydroxide (7·5 g.; 5·25 mols.) was treated with 2 drops of water and then heated until it just fused. Phenol (22 g.; 9 mols.) was added, and then gradually 5 g. (1 mol.) of 2 : 4 : 6-trichloropyrimidine. Interaction was vigorous and was completed by heating the mixture for 20 minutes at 210—220°. The whole was cooled and shaken with excess of alkali. The 2 : 4 : 6-*triphenoxypyrimidine* left undissolved crystallised from alcohol–acetone in slender needles, m. p. 156° (Found : C, 73·6; H, 4·4. $C_{22}H_{16}O_3N_2$ requires C, 74·2; H, 4·5%). Yield, almost theoretical.

2 : 4 : 6-*Tri*-p-*tolyloxypyrimidine*, obtained similarly in almost theoretical yield, formed silky needles, m. p. 118°, from alcohol (Found : C, 75·0; H, 5·2. $C_{25}H_{22}O_3N_2$ requires C, 75·4; H, 5·5%).

2 : 4 : 6-*Tri*-p-*anisoxypyrimidine*, obtained from potassium *p*-methoxyphenoxide in 80% yield, separated from alcohol in needles, m. p. 120° (Found : C, 67·1; H, 5·0. $C_{25}H_{22}O_6N_2$ requires C, 67·3; H, 4·9%).

2 : 4 : 6-*Tri*-p-*chlorophenoxypyrimidine*, obtained in 75% yield, formed clusters of stout needles, m. p. 107°, from alcohol (Found : N, 6·0; Cl, 22·8. $C_{22}H_{13}O_3N_2Cl_3$ requires N, 6·1; Cl, 23·2%).

2 : 3-*Diphenoxyquinoxaline* was prepared in a similar manner, 1 mol. of 2 : 3-dichloroquinoxaline, 3·5 mols. of potassium hydroxide and 6 mols. of phenol being used, and the main reaction completed by heating at 100—120° for 20 minutes. The diphenoxy-compound crystallised from acetone in star-shaped clusters of needles, m. p. 160° (yield, 75%) (Found : N, 9·0. $C_{20}H_{14}O_2N_2$ requires N, 8·75%). It did not combine with methyl iodide when it was heated under pressure with excess of the latter for 8 hours at 100°.

2 : 3-*Di*-p-*tolyloxyquinoxaline*, obtained in 65% yield, formed needles, m. p. 145—146°, from alcohol (Found : N, 8·2. $C_{22}H_{18}O_2N_2$ requires N, 8·2%).

2 : 3-*Di*-p-*anisoxyquinoxaline* (yield, 54%) crystallised from glacial acetic acid in minute needles, m. p. 193—194° (Found : N, 7·5. $C_{22}H_{18}O_4N_2$ requires N, 7·5%).

2 : 3-*Di*-p-*chlorophenoxyquinoxaline* (yield, 73%), when crystallised from alcohol, had m. p. 153° (Found : N, 7·1. $C_{20}H_{12}O_2N_2Cl_2$ requires N, 7·3%).

A number of attempts to replace only one of the chlorine atoms in 2 : 3-dichloroquinoxaline by phenoxyl were unsuccessful. Nitration of 2 : 3-diphenoxyquinoxaline under various conditions led to mixtures from which no individuals were isolated.

2 : 3-*Dianilinoquinoxaline* was obtained by heating dichloroquinoxaline (1 mol.) with 5 mols. of aniline under reflux for a few minutes. When the vigorous reaction was complete, excess of aniline was removed by steam-distillation after addition of alkali; the residual dianilino-derivative crystallised from glacial acetic acid in clusters of deep yellow needles, m. p. 223° (*Found* : N, 17·8. $C_{20}H_{16}N_4$ requires N, 17·8%).

2 : 3-*Di*-m-*toluidinoquinoxaline*, obtained similarly, separated from glacial acetic acid in pale yellow plates, m. p. 225° (Found : N, 16·1. $C_{22}H_{20}N_4$ requires N, 16·5%).

2 : 3-*Di*-p *toluidinoquinoxaline* formed yellow needles, m. p. 254°, from glacial acetic acid (Found : N, 16·5%).

4-*Chloro*-6-*ethoxy*-2-*methylquinoline*.—4-Hydroxy-6-ethoxy-2-methylquinoline (1 mol.), prepared by usual methods from ethyl acetoacetate and *p*-phenetidine, was heated with 1·5 mols. of phosphorus pentachloride and a little phosphoryl chloride at 145° for 1 hour. The mixture was then poured on ice and steam-distilled. The *chloro*-compound distilled in 80—85% yield and crystallised from light petroleum (b. p. 60—80°) in clusters of prismatic needles, m. p. 65° (Found : Cl, 16·15. $C_{12}H_{12}ONCl$ requires Cl, 16·05%).

4-*Chloro*-5-*nitro*-6-*ethoxy*-2-*methylquinoline*.—The last-mentioned chloro-compound (10 g.) was gradually added to 35 c.c. of nitric acid (*d* 1·5) kept at 0°. The solution obtained was poured on ice, and the whole made neutral. The precipitate formed was dried, and then crystallised from light petroleum in hexagonal prisms, m. p. 125° (yield, 90%) (Found : N, 10·8; Cl, 12·8. $C_{12}H_{11}O_3N_2Cl$ requires N, 10·5; Cl, 13·3%).

5-*Nitro*-4-p-*anisoxy*-6-*ethoxy*-2-*methylquinoline*.—The foregoing compound was condensed with potassium *p*-methoxyphenoxide by the usual method (above) and gave the 4-p-*anisoxy*-derivative as buff hexagonal prisms, m. p. 109°, from light petroleum (Found : N, 8·3. $C_{19}H_{18}O_5N_2$ requires N, 7·9%).

4-*Phenoxy*-2-*ethoxy*-2-*methylquinoline* was prepared by condensing 4-chloro-6-ethoxy-2-methylquinoline (1 mol.) with 2 mols. of phenol in presence of 1·33 mols. of potassium hydroxide by the above general method. The reaction was complete in an hour at 180—190° and the phenoxy-compound (yield, 83%) crystallised from light petroleum in star-like clusters of needles, m. p. 107—108° (Found : N, 5·05. $C_{18}H_{17}O_2N$ requires N, 5·0%). The *methiodide*, formed by heating the base with methyl iodide in a closed tube at 100° for 3 hours, separated from water in needles, m. p. 210° (Found : I, 30·1. $C_{17}H_{17}O_2NI$ requires I, 30·2%).

4-p-*Anisoxy*-6 *ethoxy*-2-*methylquinoline* forms hexagonal prisms, m. p. 115°, from light petroleum (Found : N, 4·7. $C_{19}H_{19}O_3N$ requires N, 4·6%). The *methiodide* crystallises from dilute alcohol in leaflets, m. p. 216° (Found : I, 27·9. $C_{20}H_{22}O_3NI$ requires I, 28·2%).

4-p-*Tolyloxy*-6-*ethoxy*-2-*methylquinoline*, minute cubes from light petroleum, has m. p. 134° (Found : N, 5·0. $C_{18}H_{19}O_2N$ requires N, 4·8%). The *methiodide* forms needles, m. p. 213°, from alcohol (Found : I, 30·1. $C_{19}H_{22}O_2NI$ requires I, 29·2%).

4-p-*Chlorophenoxy*-6-*ethoxy*-2-*methylquinoline* crystallises from light petroleum in rectangular prisms, m. p. 125° (Found : N, 4·8; Cl, 11·2. $C_{18}H_{16}O_2NCl$ requires N, 4·5; Cl, 11·3%). The *methiodide*, needles from dilute alcohol, has m. p. 213—214° (Found : I, 27·7. $C_{19}H_{19}O_2NClI$ requires I, 27·9%).

4-m-*Nitro*-p-*methoxyphenoxy*-6-*ethoxy*-2-*methylquinoline*.—4-*p*-Anisoxy-6-ethoxy-2-methylquinoline (10 g.) was added to a mixture of 150 c.c. of glacial acetic acid and 150 c.c. of nitric acid (*d* 1·5) at 0°. The solution was poured on ice and neutralised. The precipitate was crystallised from ethyl alcohol–light petroleum and the *nitro*-compound was thus obtained as cream needles, m. p. 183—184° (Found : N, 8·0. $C_{19}H_{18}O_5N_2$ requires N, 7·9%). The *methiodide*, needles from alcohol, melts at 224° (decomp.) (Found : I, 27·0. $C_{20}H_{21}O_5N_2I$ requires I, 27·2%). The nitro-compound could not be obtained by condensing 4-chloro-6-ethoxy-2-methylquinoline with the potassium derivative of 3-nitro-4-methoxyphenol.

4-m-*Amino*-p-*methoxyphenoxy*-6-*ethoxy*-2-*methylquinoline*, obtained from the preceding nitro-compound by reduction with stannous chloride in glacial acetic–hydrochloric acid solution, and extracted according to general practice, crystallised from alcohol in rectangular plates, m. p. 139° (Found : N, 8·6. $C_{19}H_{20}O_3N_2$ requires N, 8·6%).

4-m-*Bromo*-p-*methoxyphenoxy*-6-*ethoxy*-2-*methylquinoline*.—(*a*) The last-named amino-compound was diazotised in hydrochloric acid, and the solution added to one of cuprous bromide in hydrobromic acid. By usual procedure the *bromo*-compound was isolated, and was obtained in prismatic needles after several crystallisations from alcohol (charcoal). It melted at 193—

194° (Found: Br, 19·7. $C_{19}H_{18}O_3NBr$ requires Br, 20·6%). (b) 4-Chloro-6-ethoxy-2-methylquinoline was condensed with 3-bromo-4-methoxyphenol in presence of potassium hydroxide at 180—190°. The condensation mixture was treated with warm alkali. The tarry solid left was extracted with light petroleum (b. p. 60—80°) until it was free from unchanged chloro-compound, and then crystallised from dilute alcohol. The bromo-compound obtained melted at 193—194° alone or when mixed with the product from (a) (Found: Br, 20·2%).

UNIVERSITY OF LONDON (BEDFORD COLLEGE). [*Received, February 13th,* 1937.]

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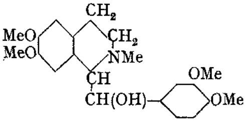
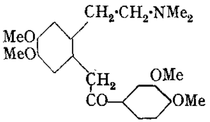
92. α- and β-*Hydroxylaudanosines. Part II. The Products of Exhaustive Methylation.*

By F. E. KING and PHILIBERT L'ECUYER.

THE recently described α- and β-hydroxylaudanosines (I) (King, L'Ecuyer, and Pyman, J., 1936, 731) not only have significance in regard to the oxidation of laudanosine but, as derivatives of this alkaloid, also possess an interest which justifies a more detailed investigation of their reactions, and a beginning has been made with the exhaustive methylation of the isomerides.

(I.)



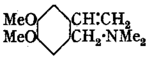


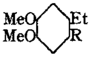
(II.)

The decomposition products of 1-benzyltetrahydro*iso*quinolinium hydroxides may in theory be two-fold, depending on which of the C–N links in the heterocyclic ring is severed, but the analogies provided by the first stages in the Hofmann degradation of laudanosine (Decker and Galatty, *Ber.*, 1909, **42**, 1179), of narcotine (Roser, *Annalen*, 1888, **247**, 169), and of hydrastine (Freund, *ibid.*, 1892, **271**, 350) suggest that ring-opening in the hydroxylaudanosines is more likely to be restricted to that position which will result in the production—through its enolic form—of the keto-base (II). Actually, an unusual reaction was found to occur.

The effect of aqueous sodium hydroxide and of silver oxide, under various conditions, on the *methiodides* and *methochlorides* of both α- and β-hydroxylaudanosines was to give a relatively volatile oil from which the *methiodide* and the *picrate* of a base, $C_{13}H_{19}O_2N$, were obtainable. When this base was extracted from the product by means of acid, the residue was veratraldehyde (recognised by derivatives which included the 2 : 4-*dinitrophenylhydrazone*), and it became apparent that the compound $C_{13}H_{19}O_2N$ was 4 : 5-*dimethoxy-2-vinylbenzyldimethylamine* (III). The novelty of the decomposition of the hydroxylaudanosine methohydroxides in comparison with others of similar constitution suggests that the initial phase in the degradation is the detachment of the veratryl nucleus; no alternative to the formation of the vinyl base (III) would then be possible.

(III.)





(IV.)

In conformity with its unsaturated character, the amine polymerised on attempted distillation, and absorbed two atoms of hydrogen when catalytically reduced, giving 4 : 5-*dimethoxy-2-ethylbenzyldimethylamine* (IV, R = $CH_2·NMe_2$). This was a liquid which was identified by its *picrate*, *methiodide*, and *methochloride*, the last being identical with the catalytic reduction product of 4 : 5-*dimethoxy-2-vinylbenzyltrimethylammonium chloride*.

Since Hofmann's method of exhaustive methylation is not applicable to amines such as (III), the second phase in the degradation was attempted by the Emde process, for which purpose the methochloride of the reduced base (IV, R = $CH_2·NMe_2$) was used.

The oil remaining when the evolution of trimethylamine had ceased was **4-*methyl*-5-*ethylveratrole*** (IV, R = Me), and on demethylation this gave the solid 4-methyl-5-ethylcatechol, which, being difficult to purify, was characterised by its crystalline *di*-p-*nitrobenzoate*.

The constitution of the ultimate degradation product was proved by a synthesis from 4-methylveratrole, conveniently prepared from veratraldehyde by the Clemmensen reduction process. The introduction of an acetyl group gave 4 : 5-dimethoxy-2-methylacetophenone (Harding and Weizmann, J., 1910, **97**, 1127), and a further application of the Clemmensen method of reduction completed the synthesis. The product was afterwards demethylated and compared with the material originating from the hydroxylaudanosines by means of the di-*p*-nitrobenzoate.

An attempted preparation of the amine (IV, R = CH_2·NMe_2) had to be abandoned because a necessary intermediate reaction—the introduction of an acetyl group into veratryl acetate—could not be accomplished.

A synthesis of 4 : 5-dimethoxy-2-ethylbenzyltrimethylammonium iodide was, however, effected. Nitration of 4-ethylveratrole in acetic acid solution gave 5-*nitro*-4-*ethylveratrole* (IV, R = NO_2), which was converted by reduction, either with tin and hydrochloric acid, or, better, by the catalytic method, into the crystalline 5-amino-4-ethylveratrole (IV, R = NH_2), characterised by an *acetyl* derivative. Diazotisation and the action of cuprous cyanide gave the related *cyano*-compound (IV, R = CN), which the action of sodium and alcohol reduced to 4 : 5-dimethoxy-2-ethylbenzylamine (IV, R = CH_2·NH_2), characterised as its *picrolonate*. Methylation with excess of methyl iodide produced the crystalline methiodide of 4 : 5-dimethoxy-2-ethylbenzyldimethylamine, which was readily identified with the corresponding salt of degradative origin.

In an attempt to obtain the free amine (IV, R = CH_2·NMe_2) from the related methochloride, the dry salt was heated under reduced pressure, for under these conditions benzyltrimethylammonium chloride, for example, yields benzyldimethylamine and methyl chloride together with benzyl chloride and trimethylamine (Collie and Schryver, J., 1890, **57**, 778). The solid distillate, however, consisted entirely of 4 : 5-*dimethoxy*-2-*ethylbenzyl chloride* (IV, R = CH_2Cl), which was subsequently prepared in one operation from 4-ethylveratrole, formaldehyde, and hydrochloric acid. It proved an ideal intermediate for the synthesis of the desired *amine* (IV, R = CH_2·NMe_2), which was formed in good yield on heating the chloride with methyl-alcoholic dimethylamine.

Experimental.

α- and β-Hydroxylaudanosine Methiodides and Methochlorides.—When heated with methyl iodide under reflux on a steam-bath for 2 hours, α-hydroxylaudanosine (7 g.), m. p. 138°, gave a *methiodide* which, after evaporation of the surplus reagent and crystallisation from alcohol, formed stout colourless prisms (10 g.), m. p. 168° (efferv.) (Found : C, 51·3; H, 6·1; I, 24·6. $C_{21}H_{27}O_5N,CH_3I$ requires C, 51·3; H, 5·8; I, 24·7%). The salt (8 g.) was digested with freshly prepared silver chloride (8 g.) and water (100 c.c.) on a steam-bath for ½ hour, and the resulting solution filtered from silver compounds and evaporated under diminished pressure. On crystallisation of the residue from alcohol, *α-hydroxylaudanosine methochloride* was obtained in colourless prisms, m. p. 165—166° (efferv.) (Found : Cl, 8·1. $C_{21}H_{27}O_5N,CH_3Cl$ requires Cl, 8·3%).

The formation of *β-hydroxylaudanosine methiodide* from the base of m. p. 108—109° (40 g.) began exothermally, and after brief heating under reflux the excess of methyl iodide was evaporated and the product triturated with cold methyl alcohol. Crystallisation from water afforded stellate clusters of large colourless prisms, m. p. 223—225° (Found : I, 24·8%). By the action of silver chloride there was obtained the *methochloride* (37 g.), which separated from alcohol in aggregates of opaque white prisms, m. p. 217—218° (efferv.) (Found : Cl, 8·2%).

Degradation of Hydroxylaudanosine Metho-salts.—(a) *With sodium hydroxide.* In the earlier experiments a solution of the methiodide (10 g.) in water (20 c.c.) was heated with aqueous sodium hydroxide (50 c.c. of 30%) in an oil-bath. The pale yellow oil liberated during 2 hours' boiling was removed in chloroform, and the solution dried with sodium sulphate and evaporated. On distillation, almost the entire product passed over as a colourless liquid (6—6·5 g.), b. p. 128°/2 mm. (Found : C, 68·0, 68·4; H, 8·4, 8·5; N, 5·2%). With alcoholic picric acid it yielded a *picrate*, which crystallised from alcohol in shining yellow thin prisms, m. p. 158—

159°, and was subsequently identified as that of 4 : 5-dimethoxy-2-vinylbenzyldimethylamine (III) (Found : C, 51·1; H, 5·1; N, 12·6; OMe, 14·1. $C_{13}H_{19}O_2N,C_6H_3O_7N_3$ requires C, 50·7; H, 5·2; N, 12·5; OMe, 14·0%). The *methiodide* of the base (III), which resulted from the vigorous reaction of the oil with excess of methyl iodide, separated from alcohol in stellate clusters of colourless prisms, m. p. 197—198° (Found : C, 46·5; H, 6·0; N, 4·3; OMe, 17·3. $C_{13}H_{19}O_2N,CH_3I$ requires C, 46·3; H, 6·3; N, 3·9; OMe, 17·1%).

On further investigation it was shown that, although no degradation occurred unless the sodium hydroxide solutions were boiled for a time, relatively low concentrations (*e.g.*, 1·2 mols. of 2%) were effective. Nevertheless, the distilled chloroform extracts, whether from α- or β-hydroxylaudanosine methiodide or methochloride, were invariably alike, each yielding the identical picrate, m. p. 158—159°, and methiodide, m. p. 197—198°. The extracted alkaline solutions on acidification gave small amounts of white precipitate, which after crystallisation from water had m. p. 181° alone or mixed with veratric acid.

(b) *With silver oxide.* A solution of α-hydroxylaudanosine methiodide (10 g.) in water (75 c.c.) was shaken in the cold with freshly prepared silver oxide (5 g.). Silver iodide was formed, and after a few minutes the liquid was filtered and boiled for ½ hour. The solution remained clear, and was accordingly evaporated under reduced pressure at 50°, a white solid being obtained, m. p. (rapidly heated) *ca.* 115° (efferv.). It showed an alkaline reaction, and was presumably the methohydroxide. When heated under diminished pressure at 75—85°, it decomposed, evolving water and leaving an oil, b. p. 128°/2 mm., which gave the already known picrate, m. p. 158—159°, and methiodide, m. p. 197—198°.

This oil was likewise obtained from the other hydroxylaudanosine metho-salts, and in order to separate its constituents, the product from β-hydroxylaudanosine methochloride (37 g.), after being washed with aqueous sodium hydroxide to remove traces of veratric acid, was distilled, and the distillate (28 g.) shaken with excess of dilute hydrochloric acid. The insoluble portion was removed by chloroform, and on distillation gave a product (12 g.), b. p. 148°/11 mm., which solidified and had m. p. 44—45° alone or mixed with veratraldehyde. Its identity was further established by the preparation of the phenylhydrazone, m. p. 120° (121°; Juliusberg, *Ber.*, 1907, **40**, 119), semicarbazone, m. p. 181° (177°; Béhal and Tiffeneau, *Bull. Soc. chim.*, 1908, **3**, 309), and 2 : 4-*dinitrophenylhydrazone*, which crystallised from acetic acid in short orange needles, m. p. 253—255° (Found : N, 16·4. $C_{15}H_{14}O_6N_4$ requires N, 16·1%).

The acid-soluble portion was liberated from the hydrochloric acid layer by neutralisation with alkali. It was a colourless oil (*ca.* 15 g.), of which specimens gave virtually quantitative yields of the picrate, m. p. 158—159°, and the methiodide, m. p. 197—198°. An attempted distillation in a high vacuum caused formation of a non-volatile resinous polymer which was acid-soluble but gave no crystalline derivatives.

4 : 5-*Dimethoxy-2-ethylbenzyldimethylamine* (IV, R = $CH_2{\cdot}NMe_2$).—A solution of the foregoing unsaturated base (3·4 g.) in alcohol (30 c.c.) was acidified with concentrated hydrochloric acid (2 c.c.) and catalytically reduced by using palladium chloride (0·4 g.). Approximately the theoretical quantity of hydrogen (350 c.c.) was quickly absorbed, and after filtration the solution was evaporated to obtain the hydrochloride of the amine (IV, R = $CH_2{\cdot}NMe_2$), which was an uncrystallisable gum and was therefore dissolved in water and decomposed by sodium carbonate. The precipitated 4 : 5-*dimethoxy-2-ethylbenzyldimethylamine* was removed by chloroform, and the solution dried with sodium sulphate and distilled; the base, a colourless oil of faint fish-like odour, had b. p. 108°/0·06 mm. (Found : C, 69·7; H, 9·3; N, 6·1. $C_{13}H_{21}O_2N$ requires C, 70·0; H, 9·4; N, 6·3%). Mixture of equivalents of the amine and picric acid in alcoholic solution produced the *picrate*, long yellow needles, m. p. 110—111° (Found: N, 12·6. $C_{13}H_{21}O_2N,C_6H_3O_7N_3$ requires N, 12·4%).

4 : 5-*Dimethoxy-2-ethylbenzyltrimethylammonium Chloride*.—(a) When methyl iodide (2 c.c.) was added to the pure base (IV, R = $CH_2{\cdot}NMe_2$) (2 g.), a vigorous reaction ensued, giving the *methiodide* (3 g.) which formed clusters of colourless needles, m. p. 209° (Found: I, 34·9. $C_{13}H_{21}O_2N,CH_3I$ requires I, 34·8%), from alcohol. A solution of the salt (2 g.) in water (45 c.c.), digested with silver chloride, gave on evaporation the *trimethylammonium chloride* as a white solid. Crystallised from alcohol, it formed long hexagonal prisms, m. p. 150—151°, of the *monohydrate* (Found: loss on drying at 115°, 6·0. $C_{13}H_{21}O_2N,CH_3Cl,H_2O$ requires H_2O, 6·2%. Found in dried material: Cl, 12·7. $C_{13}H_{21}O_2N,CH_3Cl$ requires Cl, 13·0%).

(b) From the methiodide of the unsaturated base (III) by the action of silver chloride the corresponding *methochloride* was obtained. It was very soluble in alcohol, but slowly crystallised from methyl ethyl ketone in colourless microcrystals, m. p. 218° (efferv.) (Found: Cl, 13·0. $C_{13}H_{19}O_2N,CH_3Cl$ requires Cl, 13·1%). A solution of the chloride (10 g.) in alcohol (100 c.c.)

was reduced by hydrogen in presence of platinum oxide catalyst (0·4 g.). The reaction ceased in 2 hours after approximately the required amount of hydrogen (825 c.c.) had been absorbed, and when filtered and evaporated, the solution yielded the methochloride of the amine (IV, R = $CH_2·NMe_2$), m. p. 150—151° alone or mixed with a specimen obtained as in (a).

Degradation of 4 : 5-*Dimethoxy-2-ethylbenzyltrimethylammonium Chloride by Emde's Method.*—A solution of the chloride (4 g.) in water (50 c.c.) was heated on a steam-bath and, with carbon dioxide passing through the liquid, sodium amalgam (14 g.) was added during 6 hours. After acidification with hydrochloric acid, the oily upper layer which had appeared was dissolved in benzene, which was then dried and distilled. 4-*Methyl-5-ethylveratrole* (IV, R = Me) (1·8 g.) was thus obtained as a colourless oil of distinctive odour, b. p. 105°/5 mm. (Found : C, 73·5; H, 8·9. $C_{11}H_{16}O_2$ requires C, 73·3; H, 8·9%). The oil (1·7 g.) and hydriodic acid (25 c.c., b. p. 126°) were heated in a carbon dioxide atmosphere under reflux at 140° for 1 hour. The solution was cooled, diluted with water, and shaken with chloroform; this extracted 4-methyl-5-ethylcatechol, a somewhat hygroscopic solid which was difficult to purify. When it was dissolved in pyridine and treated with *p*-nitrobenzoyl chloride (2 mols.), a vigorous reaction occurred which was completed by heating on a steam-bath for ½ hour. After the addition of water, the pale yellow solid was washed with acid, then alkali, and finally water, and crystallised from alcohol or a little ethyl acetate diluted with alcohol. 4-*Methyl-5-ethylcatechol di*-p-*nitrobenzoate* then formed colourless needles, m. p. 124—125° (Found : C, 61·4; H, 4·2. $C_{23}H_{18}O_8N_2$ requires C, 61·3; H, 4·0%).

3 : 4-*Dimethoxytoluene.*—Veratraldehyde (100 g.), prepared as by Barger and Silberschmidt (J., 1928, 2924), was heated for 15 hours with concentrated hydrochloric acid (1000 c.c.) boiling under reflux with amalgamated zinc (500 g.). After dilution with water, the reaction mixture was steam-distilled, and the distillate extracted with chloroform. The chloroform layer, dried and distilled, gave 3 : 4-dimethoxytoluene (29 g.), b. p. 110°/18 mm. (Found : C, 71·2; H, 7·9. Calc. for $C_9H_{12}O_2$: C, 71·1; H, 7·9%).

4-*Methyl-5-ethylveratrole* (IV, R = Me).—4 : 5-Dimethoxy-2-methylacetophenone (20 g.), prepared from 3 : 4-dimethoxytoluene by the method of Harding and Weizmann (*loc. cit.*), and amalgamated zinc (100 g.) were heated with concentrated hydrochloric acid (200 c.c.) boiling under reflux. After 15 hours, more acid (100 c.c.) was added, the heating being continued for a further 5 hours; the liquid was then diluted and steam-distilled. The chloroform-soluble product, 4-methyl-5-ethylveratrole, was an oil (14 g., yield 78%), b. p. 105°/5 mm. (Found : C, 73·2; H, 8·8%). Its identity with the Emde degradation product was proved by demethylation to the catechol compound, which was converted into the di-*p*-nitrobenzoate as already described, the synthetical material having m. p. 124—125° alone or mixed with a specimen originating from the hydroxylaudanosines.

Veratryl Alcohol, and Experiments with Veratryl Acetate.—A solution of veratraldehyde (25 g.) in methyl alcohol (150 c.c.) was reduced by hydrogen under pressure (maximum 2—3 atm.) with platinum oxide (0·7 g.) as catalyst. The absorption of gas (*ca.* 3,700 c.c.; 1 mol.) was rapid, and after 10 minutes all reaction ceased. The solution was then filtered (small quantities of platinum promote condensation to tetramethoxydihydroanthracene during distillation) and evaporated, and the alcohol distilled : yield, above 95% of b. p. 165°/11 mm. (compare the use of platinum-black by Vavon, *Compt. rend.*, 1912, **154**, 360; and by Carrara and Cohn, *Gazzetta*, 1926, **56**, 144) (Found : C, 64·5; H, 7·2. Calc. for $C_9H_{12}O_3$: C, 64·3; H, 7·1%).

A strongly cooled solution of the alcohol (5 g.) in pyridine (18 c.c.) was treated with acetyl chloride (2·5 g., 1·1 mols.), and after 1 hour at the ordinary temperature was poured into dilute hydrochloric acid. The brownish oil extracted by ether gave on distillation veratryl acetate, b. p. 134°/0·08 mm. A further preparation of 41 g., b. p. 168°/14 mm., was obtained by refluxing the alcohol (36 g.) with excess of acetic anhydride (cf. Vavon, *loc. cit.*; Tiffeneau and Fuhrer, *Bull. Soc. chim.*, 1914, **15**, 171) (Found : C, 62·4; H, 6·9. Calc. for $C_{11}H_{14}O_4$: C, 62·2; H, 6·7%).

The action of powdered aluminium chloride (60 g.) added in portions at intervals of 10 minutes to the acetate (30 g.) and acetyl chloride (13 g.) in carbon disulphide (1500 c.c.) occurred smoothly at room temperature, and was completed after 24 hours on a hot water-bath. The solvent was then decanted, and the product submitted to steam-distillation. The light brown solid residue could not be crystallised, and an attempted reduction by the Clemmensen process left it largely unchanged, although a small amount of a compound which crystallised from alcohol in colourless needles, m. p. 215°, was isolated (Found : C, 69·9; H, 6·8%).

5-*Nitro-4-ethylveratrole.*—4-Ethylveratrole (25 g.) (Barger and Silberschmidt, *loc. cit.*) was

added dropwise to a solution of nitric acid (15 c.c.) in water (15 c.c.) maintained at 0°. The solution darkened and became viscous, and on removing it from the freezing mixture heat was evolved. After 2 hours, the product was heated on a water-bath at 60° for 40 minutes and then poured into water. The heavy oil solidified and was collected and dried. *5-Nitro-4-ethylveratrole* distilled at 177°/12 mm. and crystallised from light petroleum in clusters of long yellow prisms, m. p. 54—54·5° (Found : C, 57·1; H, 6·1. $C_{10}H_{13}O_4N$ requires C, 56·9; H, 6·1%). In later experiments a solution of 4-ethylveratrole (25 g.) in acetic acid (25 c.c.) was added to cooled nitric acid (15 c.c.); yield 25 g., b. p. 138°/0·02 mm.

5-Amino-4-ethylveratrole.—Tin-foil (25 g.) was added in portions to a suspension of 5-nitro-4-ethylveratrole (10 g.) in concentrated hydrochloric acid (110 c.c.), and when the reaction had slackened the mixture was heated on a steam-bath for ½ hour. Water was added, and the tin precipitated by hydrogen sulphide. The amine being easily soluble in water, the filtered solution was concentrated under diminished pressure to *ca.* 100 c.c., saturated with ammonium sulphate, and basified with ammonia. The purple oil was removed by several extractions with ether, and gave 5-amino-4-ethylveratrole (3 g.) as a pale yellow liquid, b. p. 154°/3 mm., crystallising in prisms, m. p. 63°, which slowly darkened. It was characterised by the *acetyl* derivative, which crystallised from water in colourless prisms, m. p. 147° (Found : N, 6·4. $C_{12}H_{17}O_3N$ requires N, 6·3%).

The nitro-compound (20 g.) was more conveniently reduced by dissolving it in alcohol (250 c.c.) and shaking the solution with hydrogen (maximum pressure, 2—3 atm.) in contact with palladised strontium carbonate (7 g. of 5%). The theoretical amount of hydrogen (6·3 l.) was absorbed in 1½ hours, and the filtered solution was then evaporated and the residue distilled; yield of pure amine, 16 g.

5-Cyano-4-ethylveratrole.—Cuprous chloride, prepared by reducing a solution of copper sulphate (27·5 g.) and sodium chloride (9·8 g.) in hot water (90 c.c.) with aqueous sodium sulphite [from sodium bisulphite (7·6 g.) and sodium hydroxide (5·6 g.) in water (40 c.c.)], was suspended in water (50 c.c.) and treated with a solution of sodium cyanide (15 g.) in 25 c.c. of water. 5-Amino-4-ethylveratrole (16 g.), dissolved in concentrated hydrochloric acid (20 c.c.) and water (75 c.c.), was cooled in a freezing-mixture and diazotised with a solution of sodium nitrite (6·6 g.) in water (20 c.c.). The diazo-solution was neutralised with a little solid sodium carbonate, and the cuprous cyanide, cooled by crushed ice and mixed with benzene (50 c.c.), was introduced in small quantities below 0°. Vigorous stirring was continued for 5 hours at room temperature, and the mixture was then heated for ½ hour at 50°. The benzene layer was thoroughly washed (acid; alkali; water), dried, and evaporated, leaving *5-cyano-4-ethylveratrole*, which showed signs of decomposition when heated under 15 mm., but distilled at 126—127°/0·05 mm. as a straw-coloured liquid (11 g.). It solidified on cooling, having m. p. 56—58°, and crystallised from light petroleum in colourless elongated prisms, m. p. 60° (Found : C, 69·1; H, 6·8; N, 7·5. $C_{11}H_{13}O_2N$ requires C, 69·1; H, 6·8; N, 7·3%).

4 : 5-Dimethoxy-2-ethylbenzylamine.—To a solution of the cyanide (5 g.) in alcohol (90 c.c.) boiling under reflux on a steam-bath, sodium (8 g.) was added in portions of *ca.* 1 g. during 1½ hours. When all the sodium had dissolved, water (50 c.c.) was added, and the alcohol was evaporated on a steam-bath with the assistance of a stream of air. The product was extracted with ether, and the basic constituent removed from the extract by shaking with dilute hydrochloric acid, leaving in the ether a neutral oil, b. p. 51°/1 mm. (Found : C, 77·3; H, 9·9%). The acid solution was basified, and the precipitated 4 : 5-dimethoxy-2-ethylbenzylamine isolated and distilled. It was a colourless liquid, b. p. 102—103°/1 mm., and with alcoholic picrolonic acid gave a sparingly soluble *picrolonate*, crystallising in rosettes of pale yellow needles, m. p. *ca.* 235° (decomp.) (Found : N, 15·6. $C_{11}H_{17}O_2N,C_{10}H_8O_5N_4$ requires N, 15·3%).

The amine was methylated by boiling for several hours with a large excess of methyl iodide. The product, which was isolated by evaporation to dryness, was dissolved in a little alcohol, and after 2 days a crystalline deposit of 4 : 5-dimethoxy-2-ethylbenzyltrimethylammonium iodide had formed, m. p. 208° alone or mixed with the salt from the hydroxylaudanosines.

4 : 5-Dimethoxy-2-ethylbenzyl Chloride.—When heated in a high vacuum, 4 : 5-dimethoxy-2-ethylbenzyltrimethylammonium chloride gave a distillate, b. p. 128°/1 mm., consisting of *4 : 5-dimethoxy-2-ethylbenzyl chloride* (IV, R = CH_2Cl), which crystallised on cooling and had m. p. 40° (Found : C, 62·0; H, 7·0; Cl, 16·2. $C_{11}H_{15}O_2Cl$ requires C, 61·6; H, 7·0; Cl, 16·3%). It was also obtained when aqueous formaldehyde (15 c.c.; 40%) containing 4-ethylveratrole (5 g.) was boiled with concentrated hydrochloric acid under reflux for ½ hour. The oily portion darkened and became more viscous, and on cooling was extracted by ether and fractionally distilled. The first fraction (2·3 g.), b. p. 129°/1 mm., formed colourless crystals (Found :

C, 61·2; H, 7·0%), m. p. 40° alone and when mixed with the degradation product of the quaternary chloride (IV, R = $CH_2·NMe_3Cl$).

4 : 5-*Dimethoxy*-2-*ethylbenzyldimethylamine*.—On adding the foregoing chloride (1·8 g.) to a solution of dimethylamine (3 g.) in methyl alcohol (7 c.c.), heat was evolved, but the mixture was heated in a sealed tube at 120° before attempting to isolate the product. The alcohol was evaporated, the residue acidified with hydrochloric acid, and non-basic material removed by ether. An excess of sodium hydroxide added to the acid layer liberated the tertiary *amine* (IV, R = $CH_2·NMe_2$) as a colourless liquid, b. p. 108°/0·06 mm. (Found : N, 6·4. $C_{13}H_{21}O_2N$ requires N, 6·3%). The picrate, m. p. 110—111°, and the methiodide, m. p. 209°, were identified with specimens obtained in the course of the degradation experiments.

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93. *The Conductivity of Potassium Chloride Solutions.*

By CECIL W. DAVIES.

IN the recent literature of conductivity measurements much emphasis has been placed on two possible sources of error, the presence of which, it has been claimed, may vitiate all the earlier results on which our knowledge of conductivities is based. The first of these concerns the method of earthing the bridge network : Jones and Josephs (*J. Amer. Chem. Soc.*, 1928, **50**, 1049) have proposed a new method, and regard all earlier procedures as erroneous. The second is one of cell design : Jones and Bollinger (*ibid.*, 1931, **53**, 411) and also Shedlovsky (*ibid.*, 1932, **54**, 1411) have shown that in cells of the well-known Hartley and Barrett type (J., 1913, **103**, 786), as well as in the pipette cells of Washburn (*J. Amer. Chem. Soc.*, 1916, **38**, 2431), parasitic currents may flow through capacity-resistance by-paths, causing errors in the measured resistance which will vary with the size of that resistance and with the frequency of the alternating current.

On the theoretical side these two potential sources of error are established, but their actual importance in any particular series of measurements is not easy to assess, and there are grounds for thinking that criticisms (Jones *et al.*; Shedlovsky; *locc. cit.*) of the earlier work of Kohlrausch and others are unduly pessimistic. The present work was undertaken partly to throw further light on this point, and partly to explain discrepancies that exist between the careful measurements of Shedlovsky (*loc. cit.*) on dilute potassium chloride solutions, and some earlier measurements of Grindley and Davies (*Trans. Faraday Soc.*, 1929, **25**, 133). These discrepancies are attributed by Shedlovsky, in part at least, to the use by Grindley and Davies of a Hartley and Barrett cell. Actually, Shedlovsky overlooked the fact that his results were based on the absolute measurements of Parker, whilst Grindley and Davies's figures were based on the Kohlrausch standard. This difference in cell constant basis accounts for the greater part of the discrepancy, but there is a small residual effect to be explained. To achieve these objects, measurements have been made in various cells and at various frequencies on dilute potassium chloride solutions at 18° and 25° partly with the Jones and Josephs earth and partly with the bridge not earthed.

EXPERIMENTAL.

The Bridge.—The measuring bridge was similar in type to that used in the earlier work (Grindley and Davies, *loc. cit.*). The resistance box was a calibrated " non-inductive " box by the Cambridge Instrument Co., and in parallel with this was a 0·0005 microfarad variable air condenser. In a few measurements this was insufficient to balance out capacity effects, and a 0·01 microfarad condenser was available for use in parallel with it. The detector was a single telephone ear-piece of 200 ohms resistance, connected to the two ends of the bridge wire. The bridge network was not earthed in any way for the measurements reported, but for a preliminary series of measurements a Jones and Josephs earth was built up, and resistance readings were made both with and without this arrangement. In every case the two readings agreed within

the accuracy of measurement, which was better than 0·01% when the cell contained potassium chloride solutions and was about 0·1% when the cell contained conductivity water alone. The measuring bridge, as well as the thermostat and the two balances used in the work, was contained in a small room maintained at a constant temperature, about 1° lower than that of the thermostat, by thermostatically-controlled heating coils. The source of current was a valve oscillator of the type described by Woolcock and Murray-Rust (*Phil. Mag.*, 1928, **5**, 1130). This was housed in an earthed iron box some distance from the bridge, and delivered current of either 1000 or 3150 cycles. A switch was incorporated in the bridge whereby the leads from the oscillator could be interchanged (see Jones and Josephs, *loc. cit.*), but with the equipment used the resistance reading was always found to be independent of the setting of this switch, nor was it dependent upon whether the conduits carrying the leads from oscillator to bridge were or were not earthed. The procedure adopted with each resistance measurement was to set the box at a value close to the resistance of the cell and determine the two null points for the lower frequency, as described in the previous paper. This was then repeated for two more settings of the resistance box, the cell being shaken between each of the six readings. The same procedure was then repeated at the higher frequency. Normally the readings at a given frequency agreed with one another to within 0·01%.

The Cells.—Two cells were used in this work. The one used for all the measurements reported in detail was a Hartley and Barrett borosilicate cell with lightly blacked electrodes about 6 sq. cm. in cross-section and 0·7 cm. apart. The second was a similar cell with greyed electrodes. The cells when in use were supported in a thermostat filled with odourless paraffin (" chloridol "), and connection to the bridge was made through two test-tubes filled with mercury and immersed in the bath. The resistances of the leads to the cell electrodes were measured directly, and allowed for in the calculations. The runs were generally made alternately at 18° and 25°, and the thermostat was freshly set for each run by means of two standard thermometers calibrated at the National Physical Laboratory. Fluctuations in the thermostat temperature during a run never exceeded 0·005° and were normally much less.

The Conductivity Water.—The water was obtained from a still of the type described by Bourdillon (J., 1913, **103**, 791). Its conductivity varied between 0·2 and 0·8 gemmho.

The Potassium Chloride Solutions.—Four separate samples of " AnalaR " potassium chloride were used. The salt was recrystallised three or four times in glass vessels and finally from conductivity water in a platinum dish. The crystals obtained on cooling were drained as free as possible from mother-liquor, dried in a vacuum oven at 100° for 2 or 3 days, and finally heated to dull redness over an open flame. The product was neutral to indicators. The stock solutions were made by weighing about 1 g. of the salt into a small weighing bottle, which was then tipped into a suitable weight of conductivity water in a seasoned flask. The weights were corrected for buoyancy. No stock solution was used more than twice.

Measurements at 25°.—In each run the conductivity of the water was measured, and about four additions of stock solution were then made from a weight burette. The results are in Table I. Col. 1 shows the equivalent concentration, based on a molecular weight for potassium

TABLE I.

Measurements at 25°.

	$10^4/R$, corr.					
$C \times 10^4$.	at 1000.	at 3150.	true.	Λ.	Δ(2).	Δ(1).
1·9825	3·9294	—	3·9298	148·61	+0·02	+0·07
3·0907	6·1091	6·1112	6·1105	148·29	−0·03	+0·02
3·3390	6·5987	6·5998	6·5998	148·22	±0·00	+0·05
4·1381	8·1722	8·1730	8·1730	148·10	+0·07	+0·11
4·9013	9·6645	—	9·6655	147·88	+0·02	+0·05
5·2151	10·278	10·280	10·280	147·81	±0·00	+0·04
6·0093	11·824	11·827	11·827	147·58	−0·07	−0·04
8·1535	16·013	16·017	16·017	147·30	+0·02	+0·04
8·7463	17·161	17·165	17·165	147·16	−0·02	−0·01
9·8869	19·391	19·394	19·394	147·09	+0·07	+0·09
11·832	23·149	23·149	23·152	146·73	−0·02	−0·01
13·148	25·685	25·692	25·692	146·53	−0·05	−0·05
17·820	34·698	34·712	34·710	146·07	+0·02	±0·00
19·660	38·246	—	38·254	145·91	+0·05	+0·02
21·956	42·607	42·619	42·619	145·56	−0·07	−0·11
41·828	80·289	80·338	80·351	144·05	—	—
62·768	—	119·54	119·56	142·86	—	—

chloride of **74·553**; Col. 2 shows the measured conductivity of the potassium chloride at a frequency of 1000, obtained by subtracting the conductivity of the solvent, corrected where necessary for interionic attraction effects (Davies, *Trans. Faraday Soc.*, 1929, **25**, 129), from that of the solution. Col. 3 shows the corresponding figure at a frequency of 3150. At the higher concentrations the measured conductivity at 3150 cycles is consistently greater than at 1000 cycles, and the difference is of the order of magnitude to be expected on account of polarisation effects; but at resistance values greater than 300 ohms (for which the cell was primarily designed) the difference never exceeds 0·04%, and the mean difference for 34 separate measurements is 0·014%. This mean difference does not greatly exceed the random errors of the measurements, but it is probably real and is to be attributed partly to traces of polarisation, and partly to any errors that may be inherent in the design of the bridge and cell. Since it is, so far as can be judged, independent of the size of the resistance measured, and present equally in cell-constant determinations and in subsequent measurements in the same cell, it cannot lead to errors as large as 0·01% in the subsequent conductivity measurements, and it seems reasonable to conclude that the data of Kohlrausch and others, who in the past have used " dipping electrodes," are also free from serious errors due to faulty cell design. Shedlovsky (*loc. cit.*) has reported somewhat greater errors when using dipping electrodes, but his electrode leads appear to have been separated by a distance many times less than in the ordinary Hartley–Barrett cell.

The finally accepted figures shown in Col. 4 of Table I were obtained by plotting, for all the solutions studied, the difference between the readings at 1000 and 3150 cycles against the resistance, and using the smooth curve to correct the readings at 1000 cycles for polarisation. The figures in Col. 4 of the table are the mean of the conductivity at 1000 cycles corrected in this way and the conductivity at 3150.

TABLE II.

Measurements at 18°.

$C \times 10^4$.	$10^4/R$, corr.	Λ.	Δ(3).	$C \times 10^4$.	$10^4/R$, corr.	Λ.	Δ(3).
0·90987	1·5647	128·96	+0·05	9·4237	15·982	127·18	−0·08
1·4078	2·4192	128·74	+0·01	10·162	17·217	127·05	−0·12
2·2642	3·8789	128·47	−0·01	10·237	17·358	127·15	−0·01
3·0876	5·2830	128·31	+0·03	13·326	22·534	126·81	±0·00
3·5179	6·0121	128·16	−0·03	15·312	25·860	126·65	+0·04
3·6067	6·1660	128·20	+0·03	15·668	26·441	126·56	−0·01
4·9107	8·3809	127·98	+0·05	16·208	27·354	126·54	+0·01
5·3792	9·1690	127·82	−0·02	20·835	35·042	126·13	+0·02
5·8921	10·035	127·72	−0·04	22·404	37·642	126·00	+0·02
7·5131	12·775	127·51	±0·00	22·583	37·939	125·98	±0·00
8·4875	14·416	127·36	−0·02	49·815	82·653	124·42	—

Results at 18°.—The measurements at 18° were carried out in the same way and the results are in Table II, where Col. 1 shows the equivalent concentration, and Col. 2 the measured conductivity, calculated in the same way as for Col. 4 of Table I.

Measurements with Greyed Electrodes.—A number of runs at 18° and 25° were made in the cell with greyed electrodes. These need not be reported in detail; their main feature was that the readings at the two frequencies differed far more than when the cell with black electrodes was used. This difference was appreciable at all but the highest dilutions; it increased inversely as the square of the resistance and was evidently due to polarisation. It amounted to 0·1% when the resistance of the solution was 300 ohms, and its equivalent concentration was 0·001*N*. The measurements leave no room for doubt that the " greying " of electrodes is less effective in minimising the effects of polarisation than has been assumed in the past.

DISCUSSION OF RESULTS.

Jones and Bradshaw (*J. Amer. Chem. Soc.*, 1933, **55**, 1780) recently made new absolute measurements on the conductivity of potassium chloride solutions, and concluded that the figure of Parker and Parker, which Shedlovsky used as his absolute standard, is 0·028% too low. Shedlovsky has accepted the new basis, which will raise all his figures for potassium chloride by 0·04 unit. All the figures hereafter quoted are adjusted in this way, and are therefore based on the Jones and Bradshaw standard.

If the new measurements at 25° are compatible with those of Shedlovsky, it should be possible to combine Shedlovsky's equation for the equivalent conductivity of potassium chloride

$$149{\cdot}86 = (\Lambda + 59{\cdot}79\sqrt{C})/(1 - 0{\cdot}2274\sqrt{C}) - 94{\cdot}9C \quad . \quad . \quad . \quad . \quad (1)$$

with the measured conductivities shown in Table I, Col. 4, and obtain a satisfactory cell constant. This test was found to fail, the " cell constant " figures showing a definite trend with concentration in the more dilute solutions. Closer examination showed that the new measurements are quite compatible with Shedlovsky's observed conductivities, but that his equation does not agree satisfactorily with either set of observed figures at the lowest concentrations. This is illustrated in Table III, which reproduces, in Cols. 1 and 2, Shedlovsky's actual results up to 0·0033N; Col. 3 shows the difference between the observed

TABLE III.

$C \times 10^4$.	Λ.	Δ(1).	Δ(2).	$C \times 10^4$.	Λ.	Δ(1).	Δ(2).
0·32576	149·37	+0·05	−0·01	14·080	146·50	+0·03	+0·03
1·0445	148·95	+0·04	−0·01	15·959	146·30	+0·04	+0·05
2·6570	148·42	+0·06	+0·02	20·291	145·76	−0·05	−0·03
3·3277	148·23	+0·05	±0·00	20·568	145·75	−0·05	−0·01
3·5217	148·16	+0·03	−0·02	23·379	145·52	+0·01	+0·05
4·6948	147·93	+0·06	+0·02	27·848	145·04	−0·13	−0·07
6·0895	147·56	−0·04	−0·07	28·777	145·03	−0·06	+0·01
8·4200	147·27	+0·06	+0·03	32·827	144·68	−0·11	−0·02
9·2856	147·11	+0·02	±0·00	Average deviation :		0·05	0·02
11·321	146·80	−0·01	−0·02				

conductivity and that calculated from Shedlovsky's equation. For every one of the six most dilute points the difference is positive, and it seems clear from the figures in this column that, although Shedlovsky's equation fits the data fairly closely right up to a concentration of 0·1N, it is nevertheless in error by more than the probable experimental error in the more dilute solutions, and leads to a Λ_0 value that is too low. An empirical equation that has been found to agree better with Shedlovsky's results up to 0·003N is

$$\Lambda = 149{\cdot}92 - 93{\cdot}85\sqrt{C} + 50C \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

The difference between the observed values and those calculated from this equation are shown in Col. 4 of Table III.

When this same equation is applied to the new measurements, a satisfactory cell constant of 0·074986 ± 0·000005 is obtained. The extent of agreement is most clearly shown by using this cell constant value to calculate equivalent conductivities for the measurements of Table I. The values obtained are shown in Col. 5 of this table, and Col. 6 shows Δ(2), the difference between these values and those calculated from equation (2). The last column gives Δ(1), the difference between the measured values and those calculated from Shedlovsky's equation (1), and shows again the inadequacy of this equation at the lower concentrations.

Application of the cell constant derived in this way to the results at 18° gives the equivalent conductivities shown in Col. 3 of Table II, and Col. 4 shows the differences between these values and those calculated from the equation :

$$\Lambda = 129{\cdot}67 - 79{\cdot}55\sqrt{C} + 35C \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

Here 129·67 is the equivalent conductivity at infinite dilution, and 79·55 is the slope predicted by Onsager's equation. The agreement is again satisfactory, the mean difference between observed and calculated values (0·02%) being no greater than the average error in the most accurate conductivity measurements. Kohlrausch and Maltby's classical measurements on potassium chloride at 18° have been represented by the equation $\Lambda = 129{\cdot}85 - 79{\cdot}8\sqrt{C}$ (see Frazer and Hartley, *Proc. Roy. Soc.*, 1925, **A, 109,** 355; Davies, *Trans. Faraday Soc.*, 1929, **25**, 129), but this is not comparable with the new measurements, since Kohlrausch and Maltby employed the value 74·60 for the molecular weight of potassium chloride. Making the necessary corrections, and modifying the authors' solvent correction to allow for interionic forces, Kohlrausch and Maltby's two series of measurements give the values shown in the first three columns of Table IV. The next two columns give the differences between these values and those calculated from equation (3). The average difference is $0{\cdot}06_5$%, and gives the difference between the new standard of Jones and Bradshaw and the

TABLE IV.

$C \times 10^4$.	Λ_1.	Λ_2.	$\Delta(3)_1$.	$\Delta(3)_2$.	$C \times 10^4$.	Λ_1.	Λ_2.	$\Delta(3)_1$.	$\Delta(3)_2$.
1·0377	128·93	128·90	+0·07	+0·04	10·185	127·23	127·21	+0·06	+0·04
2·0543	128·64	128·65	+0·10	+0·11	20·168	126·22	126·20	+0·05	+0·03
5·1186	127·99	127·98	+0·10	+0·09	50·261	124·33	124·29	+0·13	+0·09

older standard of Kohlrausch and Holborn for (approximately) 0·01N-potassium chloride on which Kohlrausch and Maltby's measurements depended.

Finally, the measurements of Grindley and Davies may be briefly considered. Before they can be compared with Shedlovsky's measurements, allowance has to be made for the different standards employed. When this is done on the basis of the figures just discussed, there remains a discrepancy which reaches a maximum value of 0·09% at 0·0015N, the Grindley and Davies value being the smaller. This is in the direction and of the order of magnitude to be expected on account of polarisation errors, since these authors employed greyed electrodes for their work.

SUMMARY.

1. The sources of error in conductivity measurements due to faulty cell design and inadequate earthing arrangements, recently discussed by Grinnell Jones and others, have been examined experimentally, and are not considered to have caused serious errors in the past.

2. On the other hand, serious polarisation errors are to be anticipated when a cell containing greyed electrodes is used outside a very restricted concentration range.

3. The equation proposed by Shedlovsky for dilute potassium chloride solutions is criticised. A modified equation, leading to a higher Λ_0 value, is proposed.

4. New measurements on potassium chloride at 25° are in agreement with Shedlovsky's figures, and, combined with new figures at 18°, lead to the conclusion that conductivities based on the Kohlrausch standard are 0·07% higher than those based on the new standard of Jones and Bradshaw.

BATTERSEA POLYTECHNIC, LONDON, S.W. 11. [*Received, February 1st, 1937.*]

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94. *The Spontaneous Ignition under Pressure of the Simpler Aliphatic Hydrocarbons, Alcohols, and Aldehydes.*

By G. P. KANE, E. A. C. CHAMBERLAIN, and D. T. A. TOWNEND.

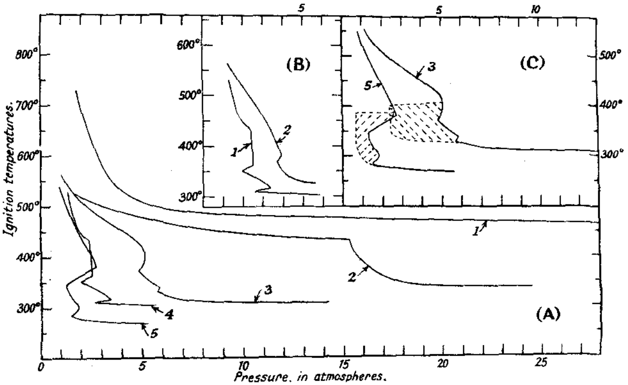
IN recent years, investigations designed to throw light on the problem of "knock" in internal combustion engines have led to the recognition that the processes involved in the combustion of complex hydrocarbons are by no means simple. For instance, Edgar and his collaborators (*J. Amer. Chem. Soc.*, 1929, **51**, 1875, 2203, 2213; 1934, **56**, 102), who studied the slow combustion of mixtures of higher paraffins, etc., with air in a flow system, found that, although initial oxidation commenced at 150—200°, becoming active between 250° and 270°, in which range the products were luminescent, and then mildly explosive between 270° and 300°, yet at higher temperatures the combustion was less intense until about 500° had been reached. Similar observations were made by Pease (*ibid.*, 1929, **51**, 1839; 1934, **56**, 2034; 1935, **57**, 2296). Subsequently, Prettre (*Bull. Soc. chim.*, 1932, **51**, 1132; cf. also Emeléus, J., 1929, 1733) made an extensive investigation into the luminescent and cool-flame phenomena associated with the slow combustion of a wide range of combustibles at atmospheric pressure. Among the paraffins, cool flames were not observed with methane and ethane; rich mixtures of propane, pentane, hexane, heptane, and octane, however, gave rise to them in a temperature range usually between 230° and 300°, above which normal inflammation did not occur until temperatures above 600° had been reached. Amylene and amyl alcohol were the simplest olefin and alcohol, respectively, to exhibit cool flames; aldehydes and ether, on the other hand, readily gave rise to them.

More recently, while studying the influence of pressure on the reactivity during slow combustion of butane–air mixtures, Townend and Mandlekar (*Proc. Roy. Soc.*, 1933, *A*,

141, 484) observed that on the attainment of a critical pressure, which varied somewhat with mixture composition, ignition occurred abruptly in a temperature range below *ca.* 350°, which in later experiments was recognised as that in which only cool flames are normally observable. It was also recognised that the critical pressure referred to was related to the critical compression ratio for the incidence of " knock " in engine practice.

The influence of pressure on the spontaneous ignition of the paraffins and other combustibles has since been systematically studied (*ibid.*, 1933, *A*, **143**, 168; 1934, *A*, **146**, 113; 1936, *A*, **154**, 95); in Fig. 1, A, the ignition-point curves for corresponding mixtures with air of methane, ethane, propane, butane, and hexane (curves 1, 2, 3, 4, and 5, respectively) have been plotted side by side for easy comparison. It will be observed that, whereas the curve for the methane–air mixture fell smoothly and showed no evidence of a lower system even at pressures up to 30 atm., and that for the ethane–air mixture showed

Fig. 1.



A. *Curves* 1, 2, 3, 4, *and* 5 *are for* 13% *methane*, 10% *ethane*, 5% *propane*, 3·8% *butane*, *and* 2·7% *hexane*, *respectively*, *in air*.
B. *Curves* 1 *and* 2 *are for* 3·8% *butane and* iso*butane*, *respectively*, *in air*.
C. *Curves* 3 *and* 5 *are as in* A, *but with cool-flame areas shaded*.

a sharp inflexion at about 15 atm. (430°), beyond which a simple lower system was superposed on the higher one, yet with all higher paraffins an abrupt fall occurred, two pressure minima of ignition being observed, one at about 280—330° and the other at about 340—370°. Another matter of importance, particularly having regard to the relation between these observations and the known knocking propensities of the hydrocarbons concerned, was that, as the paraffin series was ascended, not only did the minimum pressures requisite for ignition in the lower range progressively decrease, but the pre-ignition time-lags were also materially reduced; for instance, with propane, lags of the order of 3—5 seconds were reduced to less than 1 second with hexane. Also, to illustrate the difference in behaviour between a normal and an *iso*-paraffin, in Fig. 1, B, curves have been drawn for 3·8% mixtures of butane and *iso*butane (curves 1 and 2, respectively).

Moreover, with the members containing three or more carbon atoms, there were fairly well-defined pressure and temperature limits within which cool flames were propagated, those for the propane– and the hexane–air mixture being illustrated by the diagonally shaded areas, Fig. 1, C. When a pressure adequate for true ignition in this temperature range was attained, a two-stage process occurred, the full ignition following rapidly after the formation of a cool flame.

In considering the complex chemical processes involved in the combustion of the higher paraffins, three main conditions have therefore to be taken into account, *viz.*, (1) that giving rise to cool flames, in our own experiments somewhere in the temperature range *ca.* 280—410°; (2) that ultimately resulting in true ignition in the products arising after the passage of cool flames, there being usually two distinct zones of activity between 280—330° and 340—370° severally; and (3) that occurring above the upper temperature limit for cool flames, *i.e.*, above about 410°. It is now generally agreed that conditions conducive to (1) are mainly responsible for " knock "; the low-temperature combustion has been examined chemically, as well as by absorption spectra, and correlated with the chemical state of the charge in an engine before the passage of flame, by Egerton, Ubbelohde, and collaborators (*Proc. Roy. Soc.*, **1933**, *A*, **142**, 26; 1935, *A*, **152**, **354**; J., **1932**, **661**; *Phil. Trans.*, 1935, *A*, **234**, **433**). Knock itself probably involves essentially the processes occurring in (2), which become intense at sufficiently high pressures.

Also, there is little doubt that the processes occurring in cool flames are chain reactions and are probably associated with the presence of peroxides, aldehydes, or other active intermediate species. Aldehydes play an important rôle with the simpler hydrocarbons (cf. previous papers), but with higher members other substances also are probably concerned. Egerton and his collaborators have regarded primary peroxides as mainly responsible, and Newitt's recent discovery of the formation of mixed ethers in the slow combustion of olefins (*Proc. Roy. Soc.*, **1936**, *A*, **157**, 348) suggests another type of intermediate substance known to promote reaction (Kane and Townend, *ibid.*, in the press). The upper temperature limit for cool flames has generally been ascribed to the thermal instability of some material essential to the process and its breakdown may also involve chain reactions, but further investigation on the matter is necessary.

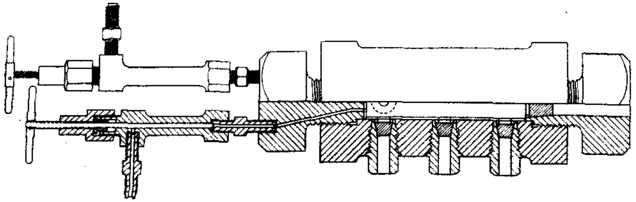
In recent discussions relating to the mechanism of the processes occurring in the low-temperature range, it has been inferred from Prettre's work that the substitution of a hydroxyl group in a paraffin would necessarily decrease chemical reactivity. It will be readily appreciated, however, from the cool-flame ranges already illustrated, that this would be a difficult issue to decide from isolated experiments carried out solely at atmospheric pressure, and as the matter is of great interest in regard to the theory of hydrocarbon combustion generally, we decided to investigate it more closely. The experiments described herein relate to the simpler corresponding paraffins, alcohols, and aldehydes containing *one, two, or three carbon atoms; with these materials chemical reactivity* has been found to ascend in the order named.

It should be added that, owing to the great violence usually associated with ignitions of combustible–oxygen media, our experiments have been restricted in the first place to mixtures made with air.

Experimental.

Explosion Vessel.—The explosion vessel (Fig. 2) is that most recently developed for use in these investigations. It was constructed of nickel–chromium steel, and provided with an

FIG. 2.



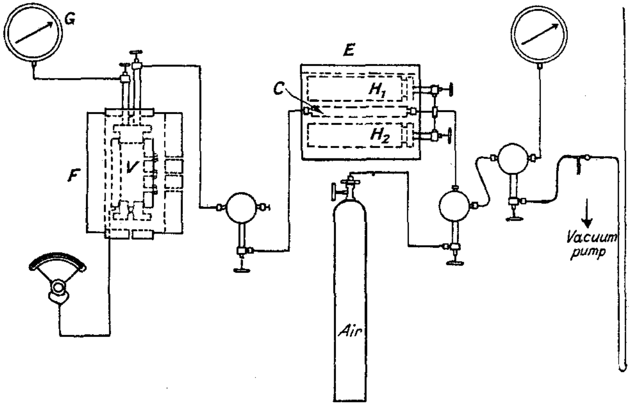
internal cylindrical cavity 15 cm. long and 3·6 cm. in diameter, closed at one end by a plug fitted with inlet and outlet valves, and at the other by a plug, either blank or alternatively provided with a quartz window, as actually shown, or with a disc recording manometer. Three

plugs for windows were also placed along a horizontal axis down one side of the vessel. The valve stems were grooved to within ½ in. of their seats, and bull-nosed so as to allow rapid admission of the gaseous mixture to the explosion vessel, and they were long enough to allow easy operation from without the heating furnace, the stuffing boxes being packed with grease-free asbestos impregnated with graphite.

Procedure.—The vessel was mounted in a well-lagged electric furnace F (Fig. 3), which could be maintained constant at any experimental temperature.

Two pressure nickel-steel vessels H_1 and H_2, fitted with slow control valves and constructed to withstand a pressure of 1000 atm., were used as storage vessels for the hydrocarbon–air mixtures, half-inch glass balls introduced into each cylinder facilitating rapid and thorough mixing of the constituents. A capacity vessel, C, from which the gas mixtures were rapidly released into the explosion vessel V, at the experimental pressure, and the pressure vessels H_1 and H_2 were separately housed in a well-lagged electric heater E, fitted with an automatic

FIG. 3.



Filling System.

temperature regulator, so adjusted that the combustible–air media under pressure were maintained homogeneously in the vapour phase. All connections and valves were wound with asbestos-covered nichrome wire, so that the system could be heated to any desired temperature up to 200°. In the case of aldehyde–air media, where storage would be undesirable, the mixtures, owing to the low b. p. of the combustibles concerned, could be made up separately for each experiment in the capacity vessel C, and after 30 seconds' agitation, they were released into the explosion vessel.

To determine an ignition point, the filling pressure was gradually raised until spontaneous ignition occurred, and then varied more carefully so that a critical value could be obtained; this pressure was usually located within 0·1 atm. above 5 atm., within 0·05 atm. between 1 and 5 atm., and within a few mm. of mercury at pressures below atmospheric. The occurrence of an ignition was conveniently recorded by the kick imparted to the Bourdon gauge G; cool flames normally gave rise to a mild pressure pulse which was easily recognised after some experience of the work. Both types of ignition were also readily distinguishable by visual observation through the quartz windows; moreover, the cool flames gave rise to intermediate products strongly aldehydic in character.

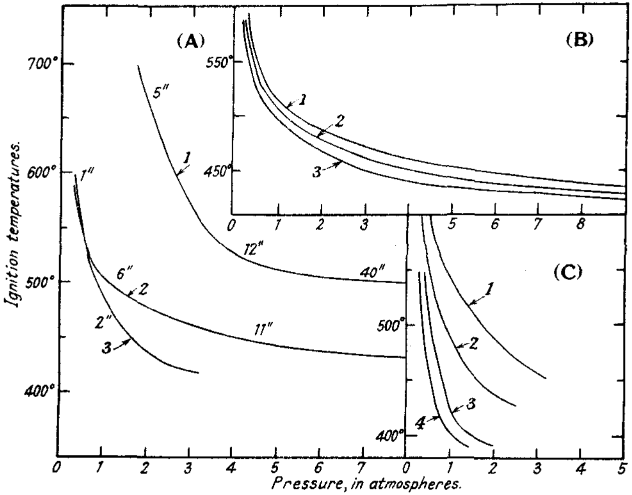
Results.

A. *Methane–, Methyl Alcohol–, and Formaldehyde–Air Mixtures.*—An account of the influence of pressure on the spontaneous ignition points of methane–air mixtures has been given else-

where (*Proc. Roy. Soc.*, 1936, *A*, **154**, 95), and their general behaviour may be judged from curve 1, Fig. 4, A (cf. also curve 1, Fig. 1), relating to a 10% mixture.

Observations with methyl alcohol (A.R. sample, dried with sodium in the usual way and fractionated, b. p. 64—65°) were restricted to three mixtures containing severally 8, 12, and 18% of the combustible (curves 1, 2, 3; Fig. 4, B). Reproducible results were not easily obtainable with the mild-steel liner usually employed in these investigations, and it was therefore replaced by one of silica. The ignition points fell progressively with increase of pressure, the general behaviour simulating that observed with methane–air mixtures, except that the time-lags (small figures along the curves) were much shorter, and the corresponding ignition pressures much lower, than with the parent hydrocarbon.

FIG. 4.



A. *Curves 1, 2, and 3 are for corresponding mixtures with air of methane, methyl alcohol, and formaldehyde.*
B. *Curves 1, 2, and 3 are for 8%, 12%, and 18% methyl alcohol–air mixtures.*
C. *Curves 1 and 2 are for 8% and 16% formaldehyde–air mixtures; curves 3 and 4 are for 8% and 16% formaldehyde–oxygen mixtures.*

Formaldehyde was prepared from paraldehyde by the method of Trautz and Ufer (*J. pr. Chem.*, 1926, **113**, 105), an apparatus similar to that of Spence and Wild (J., 1933, 1193) being used, and a special filling system being adopted so that the mixtures could be made up directly from the depolymerising apparatus. Four mixtures were investigated containing 8 and 16% of formaldehyde in air, and 8 and 16% of it in oxygen (curves 1, 2, 3, 4, respectively; Fig. 4, C). The ignition-point curves again fell quite smoothly, the ignition pressures and corresponding time-lags being now much less than with either methane– or methyl alcohol–air mixtures.

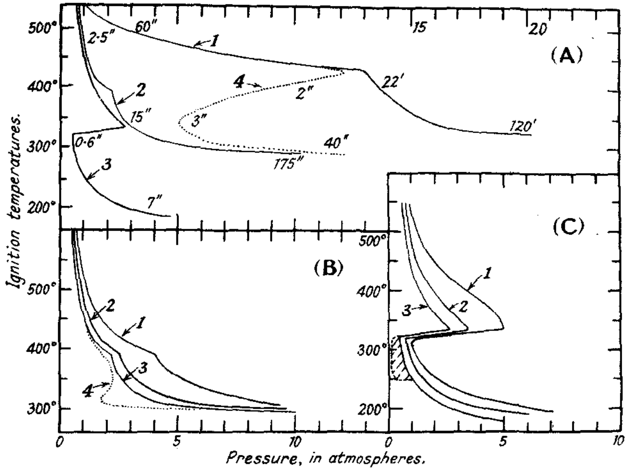
The ease of ignition of the three materials is best compared by reference to the curves for corresponding mixtures shown in Fig. 4, A. A small allowance must be made for the silica liner employed with the methyl alcohol–air mixtures, for this had the effect of lowering the ignition points by some 20° at the low and 5° at the high pressures, as compared with determinations in a mild-steel vessel.

It should be particularly noted that none of the curves shows any sign of the development

of a lower ignition system and they are typical of those of non-knocking fuels; moreover, they are in agreement with the recent observations of Bone and Gardner (*Proc. Roy. Soc.*, **1936**, *A*, **154**, 297) on the relative reactivities of equimolecular methane–, methyl alcohol–, and formaldehyde–oxygen mixtures in a static system.

B. *Ethane–, Ethyl Alcohol–, and Acetaldehyde–Air Mixtures.*—In Fig. 5, A (also cf. Curve 2, Fig. 1), the ignition-point curve (No. 1) for a 13% ethane–air mixture is reproduced and needs no further comment. The dotted curve No. 4 shows the influence of the addition of 1% acetaldehyde to this mixture (cf. *ibid.*, p. 103), and in our opinion provides strong evidence that the imposed lower system with ethane–air mixtures arises when temperature and pressure conditions allow of an adequate rate of formation and survival of acetaldehyde.

FIG. 5.



A. *Curves 1, 2, and 3 are for corresponding mixtures with air of ethane, ethyl alcohol, and acetaldehyde; curve 4 is as 1, but with addition of 1% acetaldehyde to the mixture.*
B. *Curves 1, 2, and 3 are for 4%, 6·5%, and 9% ethyl alcohol–air mixture; curve 4 is as 3, but with addition of 1% acetaldehyde to the mixture.*
C. *Curves 1, 2, and 3 are for 5%, 7%, and 10% acetaldehyde–air mixtures: shaded area denotes cool-flame limits.*

The influence of pressure on the ignition points of air–ethyl alcohol (dried in the usual way and fractionated; b. p. 78—79°) mixtures is shown by the curves 1, 2, 3 (Fig. 5, B) for mixtures containing respectively 4, 6·5 (theoretical), and 9% of the combustible. They are similar in form to those of ethane, with an inflexion in the curves at about 395°. The addition of 1% of acetaldehyde to a 9% ethyl alcohol–air mixture had an effect very similar to, but less marked than, that of a corresponding addition to the 13% ethane–air mixture, indicating that the survival of acetaldehyde probably plays a like rôle with both media. Although no cool flames had been observed with ethane–air mixtures, we were uncertain whether the alcohol–air mixtures gave rise to them under pressure, for although a mild pressure pulse was observable in certain circumstances, it was not possible to correlate this with a travelling flame, the mixture being merely luminescent; we would therefore leave the question an open one.

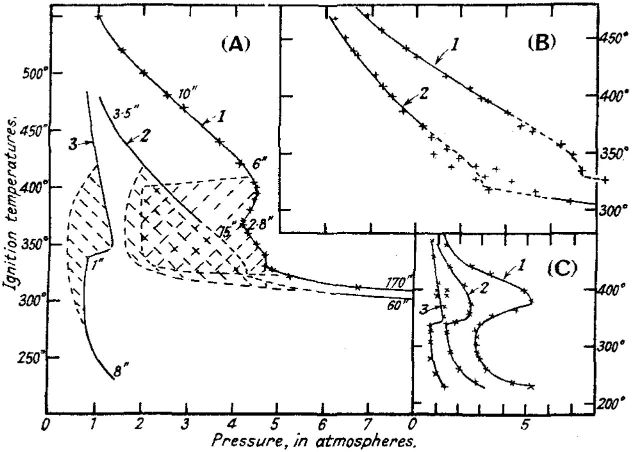
The opinion that the low-temperature system was connected with the formation of acetaldehyde found strong support when the ignition-point curves for acetaldehyde (b. p. 21°)–air mixtures were determined, as may be seen from curves 1, 2, and 3, Fig. 5, C, relating to 5, 7, and 10% mixtures, respectively. Cool flames were also now definitely observed for the first

time within the range shown by the dotted boundary curve, which relates to the 10% mixture (No. 3). Moreover, the ignition-point curves reveal a strong negative temperature coefficient of reaction at about 330°, and this seems characteristic of the upper pressure minima found in corresponding curves for all the higher paraffins and certain other combustibles.

A comparison of the three corresponding curves for ethane, ethyl alcohol and acetaldehyde (Fig. 5, A; curves 1, 2, and 3 respectively) leaves little doubt as to the order of ease of ignition of the three materials; it also appears almost certain that acetaldehyde is in some way responsible for the lower ignition system observed with ethane and ethyl alcohol.

C. *Propane-, Propyl Alcohol-, and Propaldehyde-Air Mixtures.*—Propane in admixture with air is the simplest paraffin to give rise to cool flames, and its ignition-point curves are the

FIG. 6.



A. *Curves* 1, 2, *and* 3 *are for corresponding mixtures with air of propane, propyl alcohol, and propaldehyde. Shaded areas denote cool-flame limit.*
B. *Curves* 1 *and* 2 *are for* 3% *and* 7% *propyl alcohol–air mixtures.*
C. *Curves* 1, 2, *and* 3 *are for* 3%, 5%, *and* 10% *propaldehyde–air mixtures.*

first to show two pressure minima in the low-temperature system typical of all higher paraffins (curve 1; Fig. 6, A); moreover, the processes operative in its combustion in the low-temperature system may be regarded as typical of those of knocking fuels, although it may well be that these processes are augmented when higher paraffins are concerned. It is of interest, therefore, to examine the respective behaviours of propane and propyl alcohol, for if the same order of reactivity be maintained as with the simpler paraffins already considered, ease of ignition in the lower system would seem likely to be attributable to some intermediate product common in each oxidation.

In Fig. 6, B, curves 1 and 2 relate respectively to the ignition of 3 and 7% purified *n*-propyl alcohol (b. p. 96·5—97·5°)-air mixtures. A main interest lay in the question as to whether propyl alcohol would exhibit pressure minima, as found with propane. No definite conclusion could be drawn regarding this, however, as ignitions in the range 320—360° were found to be very sensitive, and often gave different values in successive experiments; this difficulty was not overcome by replacing the mild-steel liner by silica. The broken lines, however, indicate very nearly the minimum pressures requisite for ignition in this range. Nevertheless, the values obtained were quite adequate to indicate that the propyl alcohol mixtures were more easily ignitable than those of propane, as may be seen by comparing curves 1 and 2, Fig. 6, A. It will also be observed that cool flames were propagated at somewhat lower pressures.

Propaldehyde (b. p. 50°)–air mixtures (Fig. 6, C) showed characteristics not unlike those observed with acetaldehyde, but the lower ignition system extended to rather lower temperatures.

Although the comparison between the behaviour of the three materials is not so well defined as with the ethane series, it is clear that propyl alcohol is certainly *not* less easily oxidised in the lower temperature range than propane, but it may be unwise, on the other hand, to assume that the curves justify the conclusion that the formation of propaldehyde is entirely responsible for the low-temperature combustion of both the alcohol and the hydrocarbon.

Discussion.

There are few data in the literature concerning "knock" ratings of the materials examined in this investigation, but there is general agreement between our own results and the extant observations, as may be seen from the following table:

No. of C atoms in molecule.	Critical compression ratios.		
	Paraffin.	Alcohol.	Aldehyde.
1	non-knocking		
2	14·0	7·5	both knock
3	12·0	—	

With propyl alcohol, for which no figures are available, however, although the minimum pressure for ignition in the lower range is intermediate between those of propane and of propaldehyde, we should not anticipate its knock-rating to conform to the same order; for the time-lags were much longer with the propyl alcohol between 330° and 430° than with propane. Moreover, their decrease with increase of pressure was very much less than with the paraffin, a most important consideration in correlating the knocking propensity of a fuel with ease of ignition in the lower system.

We have not yet been able to compare the respective behaviours of corresponding materials containing four carbon atoms. An attempt to determine the ignition points of amyl alcohol was only partly successful, as the ignitions were often unreproducible; it was quite clear, however, that with five carbon atoms the rate of reaction was greater with the paraffin than with the alcohol, and this is in agreement with the finding of Layng and Youker (*Ind. Eng. Chem.*, 1928, **20**, 1048), who contrasted the oxidation characteristics of heptane and heptyl alcohol. It appears probable, therefore, that a change over in the respective ease of oxidation of parent hydrocarbon and alcohol occurs with about four carbon atoms in the molecule, and the recent suggestion of Ubbelohde (*loc. cit.*) with regard to the possible function of cyclic substances in the combustion of higher hydrocarbons may possibly be of relevance in this connection.

In general, our results seem to indicate that, although intermediately formed aldehydes play an important rôle in the combustion of the lower paraffin hydrocarbons, yet their influence may be less important than that of other substances in the case of higher paraffins.

Summary.

A brief account is given of previous investigations upon the influence of pressure on the spontaneous ignition of paraffin hydrocarbon–air media, indicating the relationship between ease of ignition in a low-temperature system at *ca.* 300—350° and the knocking propensities of the fuels concerned as observed in engine practice.

In recent discussion of the chemical processes occurring in the low-temperature system and giving rise to knock, it has been assumed that aliphatic alcohols are less reactive than their parent hydrocarbons. It is now shown that, in the ethane series, ease of ignition is in the order aldehyde > alcohol > paraffin; in the propane series the same order is found, but the time-lags for the alcohol are greater than for the paraffin. With paraffins containing five or more carbon atoms, the order (from both the authors' experiments and others) is paraffin > alcohol.

The authors thank the University of Bombay, India, for a Sir Mangaldas Nathubhai Technical Scholarship (G.P.K.), and the Gas Light and Coke Company for their research Fellowship (E.A.C.C.), during the tenure of which the investigation has been carried out.

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95. *The Configuration of Heterocyclic Compounds. Part V. Thianthren and Phenoxthionine Derivatives.*

By G. M. Bennett, Mary S. Lesslie, and E. E. Turner.

It has been shown, on the one hand, from observations of polarisation in solution, that thianthren has a folded structure, whilst diphenylene dioxide is wholly planar (Bergmann and Tschudnowsky, *Ber.*, 1932, **65**, 458; Bennett and Glasstone, J., 1934, 128, 1179), and, on the other hand, by the isolation of optically active forms, that 10-methyl-, 10 ethyl-, and 10-phenyl-phenoxarsine-2-carboxylic acids possess dissymmetric molecules (Lesslie and Turner, J., 1934, 1170; 1935, 1268; 1936, 730). Of two alternative explanations of this dissymmetry, that involving the assumption of a folded structure is preferred to that requiring a stable "asymmetric tervalent arsenic atom," and it seems probable that the particularly high optical stability of the phenoxarsines mentioned is largely due to the very considerable difference in size of the oxygen and arsenic atoms.

It was nevertheless essential to prepare, and attempt the resolution of, suitably substituted thianthrens, in order to see if the undoubted folding was sufficiently stable to permit of optical activity. We have therefore prepared a *thianthren*-2(or 1)-*carboxylic acid* and have examined it from this point of view. Its crystalline l-α-*phenylethylamine* salt was repeatedly crystallised, but it appeared to be entirely homogeneous, and the acid liberated from it was optically inactive. Similarly, the base 2-aminothianthren (Krishna, J., 1923, **123**, 156) was found to yield a crystalline *d*-camphorsulphonate, but this could not be resolved. These negative results tend to confirm the conclusion recently reached as a result of a study of the isomeric sulphoxides of substituted thianthrens (Baw, Bennett, and Dearns, J., 1934, 680) in which none of the additional isomerides required by the stable folded configuration were, in fact, detected.

In phenoxthionine, according to our hypothesis, there might be an increased tendency to stable folding, since the sulphur atom is considerably larger than the oxygen atom. In fact, we found that neither 3-*nitro*-8-*methylphenoxthionine*-1-*carboxylic acid* nor *phenoxthionine*-2(or 1)-*carboxylic acid* could be resolved under the experimental conditions we employed. In view of the negative results of the resolution experiments, we did not regard it as necessary to orientate the phenoxthioninecarboxylic acid, but after this work had been completed, Suter, McKenzie, and Maxwell (*J. Amer. Chem. Soc.*, 1936, **58**, 717) described phenoxthionine-2-carboxylic acid as melting at 260—262°, whereas Mauthner (*Ber.*, 1906, **39**, 1340) had already described the 3-isomeride as melting at 223°. Our acid melted somewhat indefinitely at 230—238° and is almost certainly a pure substance, as it was prepared by recrystallisation of the *strychnine* salt and was itself repeatedly crystallised without showing signs of being a mixture.

Experimental.

Thianthren-2(?)-carboxylic Acid.—Thianthren (20 g.) was heated with phenylethylcarbamyl chloride (19 g.) and fused zinc chloride (20 g.) in an oil-bath at 160—170° for 4 hours. The mixture was boiled for 1½ hours with an aqueous-alcoholic solution of sodium hydroxide (50 g.), poured into water, heated, and filtered. Acidification of the filtrate yielded the carboxylic *acid* (average yield 1·5 g.), which was purified by dissolution in hot aqueous sodium carbonate solution and reprecipitation. It crystallised from glacial acetic acid in spherical aggregates of minute crystals, m. p. 224° (Found: C, 59·8; H, 3·1; equiv., by titration, 261·2. $C_{13}H_8O_2S_2$ requires C, 60·0; H, 3·1%; equiv., 260·2). The *amide* formed bunches of plates, m. p. 227°, from ethyl alcohol (Found: C, 60·6; H, 3·7. $C_{13}H_9ONS$ requires C, 60·2; H, 3·5%); the *anilide* separated from ethyl alcohol in radiating blade-shaped crystals, m. p. 200—201° (Found: C, 67·6; H, 4·2. $C_{19}H_{13}ONS_2$ requires C, 68·1; H, 3·9%).

Attempted Resolution of Thianthrencarboxylic Acid.—A solution of the acid (7·7 g.) with *l*-α-phenylethylamine (3·6 g.) in hot ethyl alcohol (200 c.c.) yielded on cooling and by subsequent evaporation a succession of crops of l-α-*phenylethylamine thianthrencarboxylate*, which crystallised in rectangular plates, m. p. 286—288° (Found: C, 65·7; H, 5·0. $C_{21}H_{19}O_2NS_2$ requires C, 66·1; H, 5·0%). The first crop (5·2 g.) of this salt separated in needles which had $[\alpha]_{5791}$ — 3·4°, $[\alpha]_{5461}$ — 3·8° in methyl alcohol ($l = 2$; $c = 1{\cdot}461$: $\alpha_{5791} = -0{\cdot}10°$, $\alpha_{5461} = -0{\cdot}11°$). The

second crop (after concentration of the mother-liquors; 2·7 g.) had $[\alpha]_{5791}$ − 3·5°, and a third crop had $[\alpha]_{5791}$ − 3·3°. On recrystallisation, each crop separated in rectangular plates. The first (2·2 g.) had $[\alpha]_{5791}$ − 3·4° and the second (1·0 g.) had $[\alpha]_{5791}$ − 3·3°. The acid obtained by decomposition of these various crops was in each case optically inactive.

Attempted Resolution of 2-Aminothianthren.—The base, prepared from chloronitrobenzenesulphinic acid by Krishna's method (*loc. cit.*), formed a well-crystallised salt with *d*-camphor-10-sulphonic acid, which separated from hot ethyl acetate in minute plates, m. p. 278°, but no evidence was obtained of any resolution: the colour of the solutions made polarimetric observation very difficult.

*Preparation of 3-Thiol-*p*-tolyl Carbonate.*—(a) *p*-Cresol (1 kg.), sulphonated by the method of Zincke and Kempf (*Ber.*, 1911, **44**, 413), yielded potassium *p*-cresol-3-sulphonate dihydrate (1600 g., air-dried).

(b) This salt was converted into its *O*-carbethoxy-derivative following the method of Zincke and Arnold (*Ber.*, 1917, **50**, 116) except that the proportion of water used was half that recommended by these authors, as this reduced amount accelerated the condensation and facilitated the isolation of the product. Yield, 362 g. of carbethoxy-derivative from 400 g. of potassium salt without evaporation of the mother-liquor.

(c) The potassium *O*-carbethoxy-sulphonate was heated with phosphorus pentachloride at 130° for 1 hour as recommended by Prof. S. Smiles (private communication), not for 4—5 hours as described by Zincke and Arnold (*loc. cit.*), since the shorter heating improved the yield (to over 98%) and the quality of the *O*-carbethoxy-*p*-cresol-3-sulphonyl chloride obtained.

(d) The sulphonyl chloride was reduced to the cyclic carbonate by Zincke and Arnold's method (yield 40%, not 70—80% as reported by these authors).

Preparation of 3-Nitro-8-methylphenoxthionine-1-carboxylic Acid.—The method used was Prof. Smiles's modification of Mauthner's process (*Ber.*, 1906, **39**, 1340). A solution of the thioltolyl carbonate (16·6 g., 1 mol.) and potassium hydroxide (30 g.) in aqueous alcohol (150 c.c. of water; 100 c.c. of alcohol) was boiled under reflux for ½ hour. 2-Chloro-3 : 5-dinitrobenzoic acid (24·6 g., 1 mol.), dissolved in aqueous potassium hydroxide (7·5 g. of 82% KOH, 1 mol., in 50 c.c. of water), was then gradually added, and the mixture boiled for a further ¾ hour, cooled, and filtered. The potassium salt so obtained was suspended in much hot water and decomposed with hydrochloric acid. The liberated *3-nitro-8-methylphenoxthionine-1-carboxylic acid* was dried at 100° (yield about 40%); it then crystallised from ethyl alcohol in orange clusters of slender needles, m. p. 253—254° (Found: C, 55·4; H, 3·1; N, 4·6. $C_{14}H_9O_5NS$ requires C, 55·4; H, 3·0; N, 4·6%). The dry acid provokes violent sneezing.

Attempted Resolution of 3-Nitro-8-methylphenoxthionine-1-carboxylic Acid.—To a hot solution of the acid (15 g.) in 3,500 c.c. of absolute ethyl alcohol, brucine (21·4 g.) was added. The solution, on being kept, deposited 20·6 g. of slender needles having $[\alpha]_{5791}$ − 3·4° (in chloroform). Progressive concentration of the mother-liquor gave a second crop (3·7 g.) having $[\alpha]_{5791}$ − 3·8°, and third and fourth crops having $[\alpha]_{5791}$ − 3·2° and −3·6°, respectively.

Each crop was extracted four times with 100 c.c. of boiling alcohol, and the extract allowed to cool. All the secondary crops so obtained had rotations similar to those above, and they all yielded an optically inactive acid when freed from alkaloid. The addition of less than 1 equivalent of brucine to solutions of the acid always yielded a mixture of salt with free acid and was therefore useless.

Preparation of Phenoxthioninecarboxylic Acid.—*Phenoxthionine.* The preparation of phenoxthionine was improved as follows: diphenyl ether (340 g.) was heated to 80—90°, and sulphur (64 g.) added with stirring. Anhydrous aluminium chloride (134 g.) was then added in three lots at 70°, and, after the vigorous reaction had subsided, the temperature was raised to 100° and stirring continued until no further evolution of hydrogen sulphide was observed (4 hours). The mixture was treated with dilute hydrochloric acid and extracted with chloroform, the extract dried over calcium chloride and distilled. Unchanged diphenyl ether was recovered, and 176 g. of crude phenoxthionine (yield 88% from 170 g. of diphenyl ether) obtained of b. p. 183—184°/12 mm. After two crystallisations from ethyl alcohol, it melted at 57—58° (129 g.). Suter and co-workers (*loc. cit.*) obtained 119 g. of crude phenoxthionine from 340 c.c. of diphenyl ether, and 115—116 g. of pure product.

Phenoxthioninecarboxylic acid. A mixture of 100 g. of phenoxthionine and 90 g. of phenylethylcarbamyl chloride was heated at 100°, and powdered anhydrous zinc chloride (1 mol.) added. The mixture was heated at 190—200° for 2 days, and then extracted with hot dilute hydrochloric acid. The residual tar was boiled with alcoholic potassium hydroxide, the mixture diluted, and the solution decanted from the oil. This process was repeated, and the combined

alkaline solutions, on acidification, yielded the crude acid. This was dissolved in very dilute aqueous sodium bicarbonate (the sodium salt of the acid being very sparingly soluble in water), the solution filtered, and acidified. The *phenoxthioninecarboxylic acid* (yield 20 g.) crystallised from xylene or from aqueous alcohol in needles (11 g.), m. p. 230—238° (Found: C, 64·3; H, 3·4. $C_{13}H_8O_3S$ requires C, 63·9; H, 3·3%).

When this acid was converted into its strychnine salt, the latter recrystallised from alcohol, the acid regenerated, and itself recrystallised from dilute alcohol, the acid (8·2 g.) so obtained had m. p. 230—238°.

Attempted Resolution of Phenoxthioninecarboxylic Acid.—(a) *With strychnine.* The acid (3·1 g.) was dissolved in hot alcohol, and strychnine (1·3 g.; ⅓ mol.) added. On cooling, 1·25 g. of the salt crystallised, which had $[\alpha]_{5791}$ − 8·4°, $[\alpha]_{5461}$ − 10·3° in chloroform (l = 2; $[\alpha]_{5791}$ = − 0·35°, $[\alpha]_{5461}$ − 0·43°, c, 2·087). To the heated mother-liquor a second portion of strychnine was added (1·3 g.). The crop of salt (3·1 g.) which subsequently separated had $[\alpha]_{5791}$ − 9·4°, $[\alpha]_{5461}$ − 11·5°. A third similar addition of the base to the mother-liquor gave rise to a further 1·85 g. of salt having $[\alpha]_{5791}$ − 9·3°, $[\alpha]_{5461}$ − 11·4°.

Recrystallisation of these three crops from ethyl alcohol yielded salts with approximately the same rotations, *viz.*, $[\alpha]_{5791}$ − 9·1°, $[\alpha]_{5461}$ − 10·9°. *Strychnine phenoxthioninecarboxylate* formed leaflets, m. p. 178—179° (Found: C, 69·9; H, 5·7. $C_{34}H_{30}O_5N_2S,\frac{1}{2}EtOH$ requires C, 69·9; H, 5·5%). The presence of ethyl alcohol in the dry crystals was confirmed by direct test.

(b) *With* l-α-*phenylethylamine.* The acid (15 g.) and the base (7·5 g.) were dissolved in 100 c.c. of hot ethyl alcohol. On cooling, a salt separated which had $[\alpha]_{5791}$ − 3·1°, $[\alpha]_{5461}$ − 4·1° (l = 2; c = 1·472; α_{5791} − 0·09°, α_{5461} − 0·12°) in methyl alcohol. Concentration of the mother-liquor gave successive crops with $[\alpha]_{5791}$ − 3·4°, − 4·2°, − 4·6°, and − 4·3°. Recrystallisation of the first crop gave fractions with $[\alpha]_{5791}$ varying from − 4·0° to − 4·8°. After repeated crystallisation, crops were obtained with rotations ranging from − 3·25° to − 4·6°, but the extreme specimens when decomposed gave an acid the rotatory power of which was negligible. The l-α-*phenylethylamine* salt crystallised from ethyl alcohol in needles, m. p. 188—189° (Found: C, 68·9; H, 5·3. $C_{21}H_{19}O_3NS$ requires C, 69·0; H, 5·2%).

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University of London (Bedford College).
University of Sheffield. [*Received, January* 14*th*, 1937.]

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96. *Nitrogenous Anthocyanins. Part III.* Preliminary Experiments with Betanidin.*

By A. D. Ainley and Robert Robinson.

The existence of a class of nitrogenous anthocyanins was brought to light by Willstätter, who in collaboration with Schudel (G. Schudel, Dissert., Zürich, 1918, now a very scarce publication) isolated the pigment of *Beta vulgaris* in the form of a crystalline chloride, the composition of which was not fully determined. The substance was, however, found to contain nitrogen and it was shown to be a monoglycoside on the assumption of a molecular weight comparable with that of other anthocyanins. The method of isolation involved at one stage extraction of the colouring matter from an aqueous solution by means of a mixture of amyl alcohol and acetophenone containing dichloropicric acid, a process which is not free from the danger of attachment of some chloropicryl groups to the pigment molecules. Our attempts over a period of several years to find a simpler and more direct process have met with a very limited measure of success, largely owing to the small tendency to crystallise exhibited by the members of this series and the difficulty of freeing them from organic and inorganic impurities. Willstätter and Schudel (*loc. cit.*) found that betanin could not be hydrolysed to its aglucone by means of aqueous acids without decomposition, although they obtained an alkylated salt by using alcoholic hydrochloric acid. This has also been

* Part I, J., 1932, 1439; Part II, J., 1933, 25. The title has been shortened in order to include investigations of natural products of the group.

our experience with specimens of betanin chloride isolated, in connection with another investigation, by adsorption on and elution from alumina. We have, however observed that hydrolysis occurs in a solution made by soaking sliced beet in distilled water, doubtless as the result of the action of a hydrolysing enzyme, and such solutions contain the nitrogenous anthocyanidin, which may be termed betanidin. A solution in 1% hydrochloric acid remains unchanged. After the addition of sodium chloride the colouring matter could be extracted by means of *iso*amyl alcohol and returned to a smaller volume of water after the extract had been mixed with light petroleum : this process was repeated. The aqueous solution was then evaporated under diminished pressure, and the residue extracted with alcohol. After repetition of this process the final residue was washed with water and dried in a vacuum. It was unfortunately not uncommon to sustain the loss of an entire batch from 56 lb. of beet on account of the sensitivity of the anthocyanidin to oxygen. One such loss occurred when an attempt was made to precipitate the substance from an alcoholic solution by the addition of ether. Ultimately we carried out all the operations in an atmosphere of hydrogen or nitrogen. The product was an amorphous, dark purple solid possessing a green reflex and giving 3·0% of ash on combustion. It had all the anticipated properties and was judged to be sufficiently pure to give some information on analysis. Our earlier experiences with synthetic aminoflavylium salts did not dispose us to anticipate close agreement with a theoretical value, especially that for chlorine. A frequent occurrence is the replacement of hydrogen chloride by water just as the reverse process occurs in the case of several anthocyanins. The analyses of different specimens showed fair consistency and on the assumption of a molecular weight of the same order as those of the usual anthocyanidins the molecule contains two atoms of nitrogen and loss of hydrogen chloride is indicated.

Methoxyl and methylimino-groups were not present. The carbon nitrogen ratio indicated $C_{20}N_2$ and all the results were in agreement with the formula $C_{20}H_{19-23}O_7N_2Cl,3H_2O$, in which about 30% of the hydrogen chloride was replaced by an equal weight of water. The specimens lost the equivalent of $3H_2O$ at 110° in a high vacuum, but anthocyanins are known that retain water of solvation under these conditions; hence it is uncertain that the molecule includes O_7; it may be O_6.

When hydrogen chloride was passed into a methyl-alcoholic solution of *betanidin chloride*, so as to boil the liquid, a definite change occurred in the properties of the colouring matter and analysis of the recovered salt showed that two methyl groups had been introduced. Other evidence showed that milder treatment suffices to bring about esterification and we are convinced that one of the esterified groups must be carboxyl.

The composition does not admit of the occurrence of two carboxyls unless we assume that there are only two hydroxyls in the flavylium nucleus, and from what we know of the aminohydroxyflavylium series the deep colour of betanidin could find no explanation on this basis. Therefore the formation of a second methoxyl is most probably due to etherification of a polyhydroxyphenolic section of the molecule, for example, a phloroglucinol or hydroxyphloroglucinol nucleus.

The composition and properties of betanidin chloride have led us to the speculation that it may be regarded as comprising a pentahydroxyflavylium nucleus and an ornithine residue condensed by loss of one molecule of water so as to leave four hydroxyls in the flavylium nucleus and to attach the more basic nitrogen of the ornithine directly to one of the benzene rings. Naturally, if we find that our specimens retained $1H_2O$ at 110°, there would be only three free hydroxyls in the flavylium nucleus (for example, cyanidin chloride, $C_{15}H_{11}O_6Cl$, plus ornithine, $C_5H_{12}O_2N_2$, minus $1H_2O$ gives $C_{20}H_{21}O_7N_2Cl$; or pelargonidin chloride, $C_{15}H_{11}O_5Cl$, plus $C_5H_{12}O_2N_2$ gives $C_{20}H_{23}O_7N_2Cl$ or $C_{20}H_{21}O_6N_2Cl,H_2O$). We have not obtained degradation products from betanidin, and the failure to detect even traces of phloroglucinol after fusion with alkali is perhaps significant. The investigation is being continued with the help of a process depending on adsorption of betanin on alumina.

Experimental.

Extraction and Fermentation of the Beet Pigment.—Of the several varieties of beet examined, that known as " Small globe " was rich in colouring matter and gave consistent results. Aqueous extracts of the sliced beet were acidified : the proportion that passed to butyl alcohol was very

small indeed, even after saturation of the solution with salt; the distribution to *iso*amyl alcohol was still lower; and *cyclo*hexanol extracted no pigment whatever. A mixture of butyl alcohol and acetophenone (2 : 1), with or without picric acid, extracted a small part of the colouring matter, but not to a useful extent. A solution in 1% hydrochloric acid was bluer in tone than the aqueous solution and was unchanged after 15 days. Finely sliced beet covered with distilled water slowly evolved carbon dioxide after about 8 days, the liquid became slimy and slightly bluer, and the p_H fell from 6·1 to 4·1. The betanidin produced could now be extracted by means of butyl alcohol. After purification as described below, the distribution number, equilibrated butyl alcohol–0·5% hydrochloric acid, was found to be 82 (83), and that for equilibrated *iso*amyl alcohol–0·5% hydrochloric acid was 33 (35·5). In the presence of salt the ratios are more favourable; for example, the pigment is completely transferred from aqueous solution containing salt to *iso*amyl alcohol–acetophenone (2 : 1) or *cyclo*hexanone–*cyclo*hexanol (10 : 1). On the other hand, normal anthocyanidin behaviour was not exhibited, since the colouring matter was not extracted to any extent by ethyl acetate or by ether in the presence of picric acid from a solution in acidified brine.

In some cases the fermentation of the beet solution did not occur and hence we suspected that it was due to the growth of a micro-organism. That this is the case was proved by inoculation. A mixture (4 lb. of beet and 3 l. of water) after 2 days had p_H, 6·1; already fermented solution (25 c.c.) was then added. Fermentation proceeded with evolution of carbon dioxide. The p_H was 5·6 on the third day and 4·0 on the fifth; thereafter there was a slow increase of butyl alcohol-soluble pigment, a maximum being attained on the tenth day. After some further experiments on the effects of light and air the following process was adopted.

Finely sliced beet (56 lb.) and distilled water (45 l.) were placed in enamelled buckets and covered with toluene; after 9—11 days the hydrolytic process appeared to be complete (the solutions were tested each day in respect of p_H and formation of betanidin, and inoculation was usually unnecessary). The liquid was filtered by means of a large centrifuge, each 5 l. was mixed with concentrated hydrochloric acid (80 c.c.) and sodium chloride (1500 g.) and kept for ½ hour with occasional stirring, and the aqueous solution was then separated from the toluene by siphoning and extracted with *iso*amyl alcohol (2500 c.c.). The aqueous layer was again extracted with *iso*amyl alcohol (2500 c.c.), and this alcoholic layer used for the first extraction of another 5 l. of the aqueous solution. The *iso*amyl-alcoholic extract (30 l.) was mixed with an equal volume of light petroleum (b. p. 60—80°) and shaken with water (5 l.) in a tumbling barrel; the aqueous solution was separated, saturated with sodium chloride, and extracted with *iso*amyl alcohol (5 l.). This more concentrated solution was mixed with light petroleum (15 l.) and shaken thrice with water (300 c.c. each time.) The combined aqueous extracts were washed with benzene and concentrated to a small volume under diminished pressure of hydrogen at 30—40°. The solid was collected, drained from the small residual volume of liquid (which was added to another batch), and dried in a vacuum over potassium hydroxide. It was then extracted with the minimum quantity of absolute ethyl alcohol, filtered from sodium chloride (chiefly), diluted with one-third of its volume of water, and, after addition of concentrated hydrochloric acid (2 c.c.), evaporated to dryness below 40° under diminished pressure of hydrogen (or nitrogen). This material was again taken up in absolute ethyl alcohol, the solution evaporated to dryness as before, the residue triturated with water (5—10 c.c.), and the solid *betanidin chloride* (0·2 g. from 56 lb. of beet) collected and dried in a vacuum over potassium hydroxide [Found : C, 49·0; H, 5·1; N, 5·9; Cl, 5·0; loss at 110°, 11·7. $C_{20}H_{19}O_7N_2Cl,3H_2O$ requires C, 49·2; H, 4·9; N, 5·8; Cl, 7·3; $3H_2O$, 11·1%. Found in material dried at 110° to constant weight in a high vacuum : C, 53·8, 53·8; H, 5·2, 5·1; N, 6·4, 6·3; Cl, 5·0, 5·0; MeO, 0; MeN, trace; MeC(Kuhn–Roth), 0. $C_{20}H_{23}O_7N_2Cl$ requires C, 54·7; H, 5·2; N, 6·3; Cl, 8·1%]. The significance of the analytical data has been discussed (p. 447). Crystallisation of the salts of betanidin has not yet been effected, but is still being attempted.

An aqueous solution shows the following behaviour with reagents. Sodium carbonate—the colour becomes a little more red in tone (from reddish-purple) and then brown; concentrated hydrochloric acid—slightly bluer tone; ferric chloride—brown coloration and destruction of pigment; ammonia—colour discharged to yellowish-brown; sodium hydroxide—immediate formation of a yellow solution, after 30 seconds the original colour is largely restored on acidification, after 10 minutes the colouring matter cannot be regenerated; sodium nitrite—stable; nitrous acid—immediate destruction, forming a yellow solution; barium chloride, ferrous sulphate, stannous chloride—no visible reaction; lead acetate—solution decolorised (pale yellow) and a pale pink precipitate formed, from which the colour can be partly regenerated by treatment with hydrochloric acid; basic lead acetate—no colour change.

Esterification.—Treatment of betanidin chloride with hot propyl-alcoholic hydrogen chloride completely changed the properties of the pigment. It became bluer, much more soluble in organic solvents, and more stable. The esterified salt was completely extracted from aqueous acid solution by *iso*amyl alcohol.

Betanidin chloride (57 mg.) was dissolved in absolute methyl alcohol (*ca.* 10 c.c.), and hydrogen chloride passed through the purplish-red solution until the liquid boiled; it became markedly bluer in tone. After cooling to room temperature, hydrogen chloride was again passed, but there was no apparent further colour change. After 2 hours, the liquid was added to ether (700 c.c.) and kept for 3½ hours; the colouring matter was not completely precipitated; it was collected, dried (14 mg.) in a vacuum over potassium hydroxide, and obtained as a dark purplish-black, amorphous solid with a greenish-brown lustre (Found: loss at 110°, 7·1; MeO, 11·8. $C_{22}H_{25}O_7N_2Cl,2H_2O$ requires $2H_2O$, 6·9; 2MeO, 11·5%).

Betanidin chloride (0·5 g.) was heated at 90—95° with potassium hydroxide (8 g.) and water (3 c.c.); there was vigorous decomposition and evolution of a base with a methylamine-like odour. The temperature was raised to 200—210° during 5 minutes and maintained for 2 minutes. No product could be identified, but phloroglucinol was almost certainly absent. Evidence of the presence of a pyrrole derivative was obtained in the form of a positive reaction of one of the extracts with Ehrlich's reagent, and a fatty acid resembling butyric or valeric acid in odour was produced in small quantity.

Celosia plumosa.—The flowers were extracted with 1% hydrochloric acid. The reactions of the bluish-red solution closely resembled those of a solution of betanin. The aqueous extract did not undergo fermentation with the formation of an anthocyanidin. The pigment will, it is hoped, be studied by application of the alumina method.

DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, January 14th,* 1937.]

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97. *Nitrogenous Anthocyanins. Part IV. The Colouring Matter of* Bougainvillæa glabra.

By J. R. PRICE and ROBERT ROBINSON.

IN a survey of anthocyanins (Robinson and Robinson, *Biochem. J.*, 1932, **26**, 1653; 1934, **28**, 1713) it was noted that the purple bracts of *Bougainvillæa glabra* contained a pigment resembling betanin, and a variety with scarlet bracts was found to contain a different anthocyanin of the same group. Through the kindness of Prof. A. K. Macbeth of Adelaide University, to whom we express our warmest gratitude, a considerable quantity of the dried bracts was available and it has been possible to carry out a preliminary investigation. Dr. W. S. Rapson has kindly collected further large quantities at Cape Town and the investigation will be continued; in the meantime we have established certain facts in regard to the pigment and these are now placed on record.

The greater part of the material was used up in the trial of alternative methods of isolation of the pigment, but eventually the bracts were extracted with 1% methyl-alcoholic hydrogen chloride, and the solution shaken with alumina, ammonia being added cautiously until the correct p_H was reached. The colouring matter was removed from the alumina by solution in sodium carbonate or disodium hydrogen phosphate, regenerated by acidification, and separated into anthocyanidin and anthocyanin fractions by extraction with butyl alcohol. The anthocyanidin, which may be termed *bougainvillæidin chloride*, could sometimes be crystallised from 2% hydrochloric acid; on other occasions it separated in an indefinitely crystalline or amorphous form. The analyses of different specimens were moderately consistent and showed a far higher carbon nitrogen ratio than in the case of betanidin (preceding paper). Assuming a molecule comparable with that of the anthocyanidins, it can contain only one nitrogen atom. The carbon nitrogen ratio varied from C_{20} : N to C_{24} : N, the most reliable value being C_{22} : N. This was obtained from the better analyses after allowance had been made for the methoxyl content, which was about 29% of 1MeO on the basis of the suggested formula; this methoxyl is considered to be due to partial esterification of a carboxyl group by the methyl-alcoholic hydrogen chloride used for the initial extraction. The chlorine content was again low and represented a loss of about

68% of 1HCl. Some of this loss may occur on drying in a vacuum and at 80° in a vacuum, and it must be remembered that the nitrogenous flavylium salts are now represented as containing carboxyl groups and thus may exist as betaines, the hydrochlorides of which are sometimes very unstable. A correction being made for this, the analyses are in good agreement with the formula $C_{22}H_{26-30}O_{10}NCl$, losing 68% HCl and gaining 29% CH_2. This applies to material dried at 80° in a high vacuum and it is not certain that this is anhydrous, a consideration that affects the number of oxygen atoms to be associated with the flavylium nucleus. The *N*-methyl derivative of a condensation product of delphinidin chloride or an isomeride and leucine (loss of $1H_2O$) would have the composition $C_{22}H_{24}O_8NCl$ and the occurrence of $2H_2O$ in an anthocyanidin dried at 80° is quite possible. Unfortunately decomposition occurred at higher temperatures and for this reason we were unable to establish the composition of the anhydrous substance. The distribution number of bougainvillæidin chloride (as isolated) is 50 towards equilibrated *n*-amyl alcohol–0·5% hydrochloric acid. The absorption spectrum resembles that of betanin.

Quercetin also has been isolated from the bracts.

Experimental.

Extraction of the Bracts.—The bracts of the variety most commonly grown in S. Australia (exact variety unknown) were dried on wire-gauze trays in a rapid stream of air at 45° for 24 hours or more. The material was powdered and stored in sealed containers; it suffered little change in transit. The powder (1000 g.) was placed in a 10 l. aspirator bottle and covered with 1% methyl-alcoholic hydrogen chloride. The solution was drawn off periodically from the bottom and replaced with fresh solvent; after 1—4 days the whole of the solution was drained away and a fresh extract was made which was used to start the extraction of a second kilogram of the bract powder. The first extract (*ca.* 6 l.) was mixed with ether–light petroleum (2 : 1), the colouring matter being almost completely precipitated. After a few hours, the liquid was decanted, the residue dissolved in 1% methyl-alcoholic hydrogen chloride, and the pigments reprecipitated from the filtered solution. This operation was carried out from five to eight times in different experiments. The viscous, intensely bluish-red residue was dried over calcium chloride in a vacuum desiccator and obtained as a dark purple solid. The yields were variable [26 g., 66 g., 70 g., and (from 1400 g.) 77 g.], probably depending on the time expended in the first extraction.

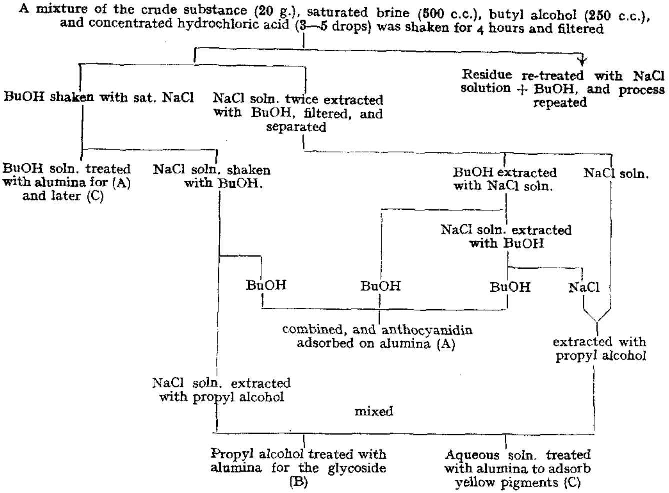
The crude substance was insoluble in benzene, chloroform, ether, ethyl acetate or acetic acid, partly soluble in propyl alcohol, and readily soluble in methyl and ethyl alcohols. It was not completely soluble in water or dilute acids and the addition of salt increased the proportion of insoluble material. The solution in brine contained a mixture of monoglycoside and diglycoside; the distribution to *iso*amyl alcohol was negligible, that to butyl alcohol was higher but still quite low. With propyl alcohol the greater part of the pigment could be extracted from saturated brine, but there remained a small part, considered to be diglycosidic, that could not be extracted. The precipitated pigment had non-glycosidic character and a useful step in the purification of this fraction was to shake the crude extract with butyl alcohol and brine. A considerable amount of impurity, insoluble in butyl alcohol, was eliminated at the same time. The crude product contained much material of high molecular weight (protein, polysaccharide). No crystalline salts, such as picrate, perchlorate, or ferrichloride, could be precipitated and in the crude form the colouring matter was very unstable both in acid and in alkaline solution.

The first attempted purification was by means of extraction with *cyclo*hexanone and picric acid; the colouring matter could be concentrated in this way, but the method was wasteful and was abandoned.

Adsorption of the Pigments on Alumina.—Chromatographic adsorption in a column of alumina (Merck's, *nach* Brockmann) gave two well-defined zones, an upper deep purple and a lower bright yellow. It was not practicable to separate the anthocyanidin from the anthocyanin in this way, although the latter was more completely adsorbed from alcholic than from aqueous solutions. The yellow pigment was a mixture of a glucoside with its aglucone.

On the basis of the preliminary experiments several schemes of purification were tried: that finally adopted is shown in the diagram. The solutions used for adsorption were all neutralised and adsorption was carried out by shaking with successive small quantities of the alumina. The treated alumina was well washed with water and methyl alcohol until the washings were colourless. The extraction with propyl alcohol was used, as it gave a good separation of mono-

from di-glycoside, and the latter was discarded; also the adsorption was very effective from the propyl-alcoholic solution.



An analysable product has not yet been isolated from (B), but since adsorption of the more readily accessible beet colouring matter on alumina from methyl-alcoholic solution has afforded the glucoside, not the anthocyanidin, and as the material thus purified possesses considerable stability, we are concentrating on this aspect of the problem. The experiments described below refer to (A) and (C).

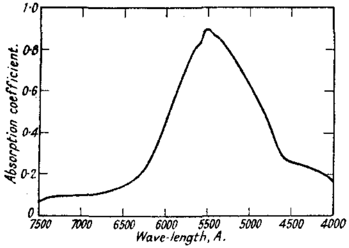
Separation of Bougainvillæidin Chloride.—The colouring matter could be eluted from the alumina by methyl-alcoholic or aqueous hydrogen chloride, but the methods were wasteful owing to decomposition. A specimen thus prepared and further purified by evaporation of the solution and repeated extraction with alcohol, followed by evaporation, was analysed with results similar to those cited below, but the purity was certainly not equal to that achieved later. Aqueous sodium carbonate or ammonia was much better than an acid reagent, but there was a tendency to decomposition when the liquid was heated to effect solution of the colouring matter. This disadvantage was overcome by the use of disodium hydrogen phosphate (7·5%, $Na_2HPO_4,12H_2O$), a hot solution of which removed all the colouring matter without decomposition.

The sodium phosphate extract was saturated with sodium chloride, filtered, acidified with hydrochloric acid, and extracted with butyl alcohol, and the butyl-alcoholic layer was shaken with a little water and just sufficient sodium carbonate to effect transference of the colour to the aqueous solution. These processes were repeated and on acidification of the concentrated aqueous solution a semi-crystalline precipitate was thrown down; this crystallised from 2% hydrochloric acid in black needles possessing a green reflex. Specimens (i and ii) from two different preparations were dried in a vacuum desiccator [Found in (i) and (ii): loss at 80° in a high vacuum, 10·8, 10·7% respectively. Found in (i), dried at 80°: C, 55·28; H, 6·13; N, 2·93%. Found in (ii), dried at 80°: C, 55·57; H, 5·64; N, 2·66; MeO, 1·36%].

A third specimen (iii) was prepared by a simplified process. The bracts were extracted during 3 days and the solution was shaken with alumina, ammonia being cautiously added until adsorption of pigment occurred. The elution was by means of cold aqueous sodium carbonate (the pigment not removed in this way was dissolved in dilute hydrochloric acid and, after neutral-

isation, re-adsorbed on fresh alumina) and the pigment was passed to butyl alcohol as described above (the glycosides remained in the acid aqueous solution). The further treatment was as above, and the yield from the bracts was about 0·1%. The substance obtained in this way did not crystallise, or at least the crystals were of very indefinite form, but it was purified by three solutions in, and separation from, 2% hydrochloric acid and dried in a vacuum over phosphoric oxide (Found: loss at 80° in a high vacuum, 5·5%. Found in material dried at 80°: C, 55·36; H, 4·96; N, 3·03; Cl, 2·32; MeO, 1·83%).

Bougainvillæidin chloride dissolves in hydrochloric acid to a deep purple solution, which becomes bright red on neutralisation; the addition of more alkali causes a change of colour through blue and violet to yellow. The distribution number with equilibrated *n*-amyl alcohol and 0·5% hydrochloric acid was 50·0. The absorption in the visible region was determined with a solution of 1·636 mg. in 25 c.c. of 0·05% methyl-alcoholic hydrogen chloride in a 2 cm. cell. The curve (see figure) shows points of similarity with those of crude betanin and the pigment of *Atriplex hortensis* (cf. Robinson and Robinson, J., 1932, 1439).



Discussion of the Analytical Results.—The average estimations for the three specimens are: C, 55·40; H, 5·58; N, 2·87; Cl, 2·32; MeO, 1·85%. On the basis of a formula containing one nitrogen atom, 1MeO corresponds to 6·35%. In harmony with our conception of the underlying chemistry and also in view of the method of preparation, we may assume that this material is a mixture of a certain substance with about 29% of its methyl derivative. Then, if all the substance had been methoxyl-free, the figures would be: C, 55·15; N, 2·90%. This gives the ratio C : N as 22·2 : 1. The value for chlorine is low, indicating loss of hydrogen chloride, and correcting for the chlorine content, and calculating for the methoxyl-free, chlorine-free base, we find C, 56·51; N, 3·0%. The carbon value is regarded as the more accurate and from this the molecular weight found is 467. From this we find $C_{22}H_{27}O_{10}N$ (*M*, 465) to be the best formula for the free base. The next stage is to note that the ratio MeO : Cl is almost 1 : 1, and this suggests that our specimens were mixtures of about 2 parts of bougainvillæidin (betaine) with about 1 part of bougainvillæidin methyl ester chloride [$2(C_{22}H_{23}O_8N,2H_2O)$, $C_{23}H_{26}O_8NCl,2H_2O$, or $C_{67}H_{84}O_{30}N_3Cl$ requires C, 55·6; H, 5·8; N, 2·9; Cl, 2·5; MeO, 2·15%, in good agreement with the analytical results]. This hypothesis is inherently probable from the chemical point of view, because methylation of the carboxyl group greatly reduces the ease of betaine formation. Phenol-betaines would still be possible, but these are not stable in acid solution in the flavylium series. Similar formulæ based on $C_{22}H_{23}O_7N$ (for example, anhydro-cyanidin-leucine) are also feasible (H, 6·2%), but require $3H_2O$ to be retained at 80°. Formulæ based on $C_{22}H_{23}O_6N$ are improbable.

Isolation of Quercetin.—The alumina (C, p. 451) on which the yellow colouring matters were adsorbed was extracted with 5% methyl-alcoholic hydrogen chloride, the filtered solution mixed with a little water, and the methyl alcohol and some of the water removed under diminished pressure. The brown solid that separated was collected and extracted with ether (Soxhlet), and the crude product precipitated from the concentrated ethereal solution by the addition of light petroleum. It was crystallised from aqueous alcohol and then from alcohol–benzene, forming yellow needles, m. p. 308—310°, and m. p. 309—311° when mixed with synthetic quercetin, m. p. 310—313°. The identity was confirmed by a comparison of dyeing properties on cotton mordanted with iron and aluminium (weak and strong), and the results were identical. Further, an acetyl derivative was prepared from the two specimens as follows. A mixture of the colouring matter or quercetin (0·3 g.) with acetic anhydride (4 c.c.) and pyridine (2 drops) was kept for 1 hour at room temperature. The product crystallised from aqueous acetone in colourless needles, m. p. 169—170° (from the colouring matter, m. p. 166—168°; from synthetic quercetin, m. p. 167—168° when mixed). There is some doubt as to the composition of this derivative (cf. Perkin, J., 1899, **75**, 449; Kubota and Perkin, J., 1925, **127**, 1889), and the question of the acetyl derivatives of quercetin is being re-investigated. The penta-acetate was also prepared from the *bougainvillæa* pigment, m. p. 191—193° after crystallisation from acetone–alcohol, m. p. 192—194° when mixed with penta-acetylquercetin, m. p. 194—195°.

The brown solid not extracted by ether in the Soxhlet apparatus could not be crystallised; it probably consisted of decomposition products of bougainvillæidin, because the yellow pigments increased in amount when the solutions constituting the first extracts were kept.

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DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, January 14th*, 1937.]

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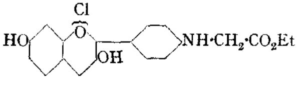
98. *Nitrogenous Anthocyanins. Part V. Synthesis of Substituted Aminoflavylium Salts.*

By A. D. AINLEY and ROBERT ROBINSON.

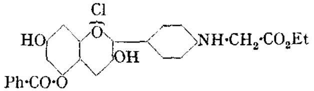
WHEN it became clear that the nitrogenous anthocyanins comprise a flavylium salt nucleus combined with an amino-acid residue, synthetical work directed to the preparation of typical substances of this kind was initiated. The problem proved to be a very difficult one, but some progress can be reported.

After a number of unsuccessful attempts in other directions, 4-amino-ω-acetoxyacetophenone (Robinson and Robinson, J., 1932, 1442) was converted into *4-carbethoxymethylamino-ω-acetoxyacetophenone*, $CO_2Et\cdot CH_2\cdot NH\cdot C_6H_4\cdot CO\cdot CH_2\cdot OAc$ (I) by treatment with ethyl bromoacetate in the presence of sodium iodide. On condensation with β-resorcylaldehyde in dioxan solution with the help of hydrogen chloride, *4'-carbethoxymethylamino-3 : 7-dihydroxyflavylium chloride* (II) was obtained.

The ketone was also condensed with 2-*O*-benzoylphloroglucinaldehyde and hydrogen chloride in ethyl acetate solution with formation of *4'-carbethoxymethylamino-3 : 7-dihydroxy-5-benzoyloxyflavylium chloride* (III).



(II.)



(III.)

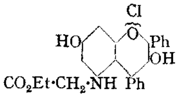
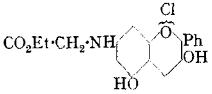
These experiments appeared to clear the ground for an attempt to synthesise an isomeride of betanidin in which the nitrogen would be attached at position 4' or at some other position in the side-phenyl nucleus. We were, however, desirous of extending such preliminaries to derivatives of 5- and 7-aminoflavylium salts, and we have not yet been successful along the ordinary lines. Thus we have not been able to obtain a suitable derivative of 6-amino-2 : 4-dihydroxybenzaldehyde, although work in this direction is still in progress.

Phloroglucinol condensed with ethyl aminoacetate with formation of *ethyl 3 : 5-dihydroxyphenylaminoacetate*, $C_6H_3(OH)_2\cdot NH\cdot CH_2\cdot CO_2Et$, but the attempt to introduce the formyl group failed.

An indication of a method of attack has, however, been obtained by the synthesis of two flavylium salts of the required type by an adaptation of the new method of condensation of polyhydroxyphenols with unsaturated ketones in the presence of chloranil and hydrogen chloride (Robinson and Walker, J., 1934, 1435; 1935, 941). If such a substance as phenyl methyl diketone, $Ph\cdot CO\cdot CO\cdot CH_3$, reacted in the tautomeric form, $Ph\cdot CO\cdot C(OH){:}CH_2$, it would come within the scope of this synthetic method. The reaction has been found to take the anticipated course in two cases, and this interesting resource will be further explored.

Condensation of ethyl 3 : 5-dihydroxyphenylaminoacetate with phenyl benzyl diketone in alcoholic solution in the presence of chloranil and hydrogen chloride afforded 5(or 7)-*carbethoxymethylamino*-3 : 7(or 5)-*dihydroxy-4-phenylflavylium chloride* (IV), and phenyl methyl diketone, treated in the same way, gave rise to 7(or 5)-*carbethoxymethylamino-*

3 : 5(or 7)-*dihydroxyflavylium chloride* (V). The alternative constitutions are represented in (IV) and (V), and (V) might be constituted like (IV), or (IV) like (V).

(IV.)   (V.)

EXPERIMENTAL.

Ethyl 4-*Carbethoxyphenylaminoacetate*.—Dry hydrogen chloride was passed into a suspension of 4-carboxyphenylglycine (10 g.) in alcohol (150 c.c.) until complete solution was effected. After a few hours the liquid was added to water (1 l.), stirred, and kept until separation of solid was complete. The *product* crystallised from light petroleum (b. p. 40—60°) in stout, very pale yellow prisms (6·0 g.), m. p. 63—63·5° (Found : C, 61·9; H, 6·9; N, 5·7. $C_{13}H_{17}O_4N$ requires C, 62·1; H, 6·8; N, 5·6%). No use could be made of this compound in directions which it is unnecessary to describe in detail; neither could the acid chloride of ethyl *N*-4-carboxyphenyl-*N*-methylaminoacetate be obtained. We were unable to introduce the chloroacetyl group in the *p*-position to nitrogen in ethyl *N*-phenyl-*N*-methylaminoacetate or ethyl *N*-acetyl-*N*-phenylaminoacetate, although several methods were tried in each case.

ω-*Chloro*-4-p-*toluenesulphonamidoacetophenone*.—A solution of ω-chloro-*p*-aminoacetophenone (4·1 g.) and *p*-toluenesulphonyl chloride (5·0 g.) in pyridine (50 c.c.) was stirred at 0° for 30 minutes. The mixture was added to dilute hydrochloric acid; the paste that separated gradually solidified. The *substance* crystallised from alcohol (charcoal) in pale yellow prisms (6·0 g.), m. p. 184° (Found : N, 4·6. $C_{14}H_{14}O_3NClS$ requires N, 4·5%).

4-p-*Toluenesulphonamido*-ω-*acetoxyacetophenone*.—A mixture of 4-amino-ω-acetoxyacetophenone (1 g.) and *p*-toluenesulphonyl chloride (1·2 g.) was shaken for 5 minutes with a little pyridine, and the reaction completed by heating for 5 minutes on the steam-bath. The *product* crystallised from aqueous alcohol in long, thin, rectangular plates (1·5 g.), m. p. 179—179·5° (Found : C, 58·7; H, 4·9; N, 4·1; S, 9·2. $C_{17}H_{17}O_5NS$ requires C, 58·8; H, 5·0; N, 4·0; S, 9·0%).

4-p-*Toluenesulphonamido*-ω-*hydroxyacetophenone*.—Ethyl bromoacetate (0·5 g.) and ether (1—2 c.c.) were added gradually to a stirred solution of 4-*p*-toluenesulphonamido-ω-acetoxyacetophenone (1 g.) in aqueous sodium hydroxide (10 c.c. of 8%). After 30 minutes' stirring, the mixture was added to 7% hydrochloric acid (25 c.c.), and the solid collected (0·9 g.); it crystallised from alcohol in very pale yellow, long, thin plates, m. p. 202—204° (decomp.) (Found : C, 58·8; H, 4·9; N, 4·8; S, 10·6. $C_{15}H_{15}O_4NS$ requires C, 59·0; H, 4·9; N, 4·6; S, 10·5%). The *substance* could not be employed for the desired purpose.

4-*Carbethoxymethylamino*-ω-*acetoxyacetophenone* (I).—Ethyl bromoacetate (8·5 g.) was added to a solution of sodium iodide (8·5 g.) in acetone (70 c.c.) and when the reaction was complete 4-amino-ω-acetoxyacetophenone (10 g.) was added to the filtered liquid, which was then refluxed for 15 hours. The product was added to water (100 c.c.), the mixture boiled, and filtered, and the residue extracted four times with boiling water–alcohol (5 : 1). The solid (2 g.) that separated on cooling crystallised from alcohol in pale yellow needles, m. p. 113° (Found : C, 60·5; H, 6·2; N, 5·0. $C_{14}H_{17}O_5N$ requires C, 60·2; H, 6·1; N, 5·0%).

4′-*Carbethoxymethylamino*-3 : 7-*dihydroxyflavylium Chloride* (II).—A solution of carbethoxymethylaminoacetoxyacetophenone (0·5 g.) and β-resorcylaldehyde (0·25 g.) in dry dioxan (15 c.c.) was saturated with hydrogen chloride at 0° for 3½ hours, kept at 0° for 13 days, filtered, and poured into ether (250 c.c.). The dark bluish-red flocculent precipitate (0·45 g.) crystallised from alcohol–ethyl acetate (1 : 3) in compact clusters of very slender needles (Found : loss at 110° *in a high vacuum*, 10·2. *Found in dried material* : C, 60·9; H, 4·6; N, 3·9; Cl, 9·6. $C_{19}H_{18}O_5NCl,2{\cdot}5H_2O$ requires H_2O, 10·6%. $C_{19}H_{18}O_5NCl$ requires C, 60·7; H, 4·8; N, 3·7; Cl, 9·3%).

4′-*Carbethoxymethylamino*-3 : 7-*dihydroxy*-5-*benzoyloxyflavylium Chloride* (III).—Hydrogen chloride was passed into a solution of carboxymethylaminoacetoxyacetophenone (1 g.) and 2-*O*-benzoylphloroglucinaldehyde (1 g.) in ethyl acetate (80 c.c.) at 0° until saturated and the mixture was kept for 12 hours at 0°, again saturated with hydrogen chloride, and kept at 0° for 12 days. After filtration from a light-coloured precipitate the deep bluish-violet solution was added to ether, and the purplish-black, deliquescent precipitate (0·58 g.) collected. A solution in alcohol–ethyl acetate (1 : 2) gradually deposited crystals when kept at 0° for 2 days. The

clusters of very dark purple, slender needles had a green reflex (Found : loss at 110° in a high vacuum, 6·9, 7·0. Found in dried material : C, 63·0 ; H, 4·7 ; N, 3·0 ; Cl, 7·7. $C_{26}H_{22}O_7NCl,2H_2O$ requires H_2O, 6·8%. $C_{26}H_{22}O_7NCl$ requires C, 63·0 ; H, 4·4 ; N, 2·8 ; Cl, 7·2%).

By using *o*-vanillin as the aldehyde component, an analogous salt was obtained (dioxan–ethyl acetate as solvent) ; it crystallised from acetic acid, containing a trace of hydrogen chloride, in small plates, brown-red by transmitted light and exhibiting a blue metallic reflex (Found : N, 3·8. Calc. : N, 3·6%).

2-O-p-*Toluenesulphonylphloroglucinaldehyde*.—Several methods for the preparation of this substance were tried ; some failed altogether and none gave good results. It will suffice to say that phloroglucinaldehyde (2 g.) was treated with *p*-toluenesulphonyl chloride and 10% aqueous potassium hydroxide in acetone solution at − 2° to + 2°. The product was dissolved in chloroform, and the solution mixed with ether and extracted with aqueous sodium carbonate. The extract was acidified, and the product taken up in ether and eventually crystallised from chloroform–light petroleum and from benzene ; it formed slightly brownish, thick prisms (0·2 g.), m. p. 130° (Found : C, 54·5 ; H, 3·9 ; S, 10·4. $C_{14}H_{12}O_6S$ requires C, 54·5 ; H, 3·9 ; S, 10·4%). This *substance* was prepared in order to attempt the direct introduction of substituted ammonia residues by replacement of the *p*-toluenesulphonoxy-group. In view of the difficulty of the preparation, the project was not pursued.

Ethyl 3 : 5-*Dihydroxyphenylaminoacetate*.—This substance could not be obtained from phloramine by interaction with ethyl iodoacetate. A solution of anhydrous phloroglucinol (10 g.) and ethyl aminoacetate (8 c.c.) in alcohol (24 c.c.) was kept under nitrogen for 3 days and then concentrated under diminished pressure over sulphuric acid. The magma of almost colourless prisms was washed with water and dried (10·8 g., m. p. 150—154°). The *substance* was readily soluble in ethyl alcohol, moderately readily soluble in ether and hot water, and sparingly soluble in cold water. It crystallised from water in short thick prisms, m. p. 153·5—154° (Found : C, 56·7 ; H, 6·3 ; N, 6·9. $C_{10}H_{13}O_4N$ requires C, 56·9 ; H, 6·3 ; N, 6·6%). The reaction can also be carried out in aqueous solution with about the same results.

Various attempts to introduce the formyl group were made and in one case, using the triacetyl derivative with hydrogen cyanide and aluminium chloride, a product yielding a *p*-nitrophenylhydrazone was isolated, but the yield was so small that the work was abandoned.

5(or 7)-*Carbethoxymethylamino*-3 : 7(or 5)-*dihydroxy-4-phenylflavylium Chloride* (IV or like V).—A well-shaken mixture of ethyl 3 : 5-dihydroxyphenylaminoacetate (2·1 g.), phenyl benzyl diketone (2·2 g.), chloranil (2·5 g.), and ethyl-alcoholic hydrogen chloride (40 c.c. of 12%) became dark mauve after 3 hours and the chloranil passed into solution. After 2 days the dark brown liquid was filtered into ether and the product (2·05 g.) was collected and washed with anisole (15 c.c.) containing a trace of hydrogen chloride. The crude product (1 g.) was dissolved in ethyl-alcoholic hydrogen chloride (24 c.c. of 2%) and slowly diluted with ether, by means of the vapour, a very dark purple, almost black, powder consisting of microscopic plates (0·8 g.) being obtained (Found : C, 60·1 ; H, 5·2 ; N, 3·0. $C_{25}H_{22}O_5NCl,2{\cdot}5H_2O$ requires C, 60·4 ; H, 5·4 ; N, 2·8%). The *substance* showed the general character of an aminoflavylium salt. The alcoholic solution is reddish-mauve and on dilution becomes nearly colourless ; addition of hydrochloric acid causes partial regeneration of the violet colour. On addition of sodium carbonate to an alcoholic solution the colour becomes browner and duller ; sodium hydroxide gives a reddish-brown solution. The salt is insoluble in water and very sparingly soluble in hot dilute 1% hydrochloric acid to a faintly violet solution.

7(or 5)-*Carbethoxymethylamino*-3 : 5(or 7)-*dihydroxyflavylium Chloride* (V or like IV).—The foregoing preparation was repeated, phenyl methyl diketone (1·5 g.) being substituted for the phenyl benzyl diketone. During 5 days the mixture became dark purple ; the liquid was filtered and mixed with ether, giving 1·4 g. of a purplish-black precipitate. This, treated as in the foregoing example, was obtained as a black powder of microscopic thin prisms, which were dark brownish-purple by transmitted light (Found : C, 53·3 ; H, 5·3 ; N, 3·4.* $C_{19}H_{18}O_5NCl,3H_2O$ requires C, 53·1 ; H, 5·6 ; N, 3·3%). The *salt* showed the general character of its class.

The reddish-violet solution in hot 1% hydrochloric acid is not completely extracted on shaking with *iso*amyl alcohol. The violet solution in alcohol is partly decolorised on dilution and the colour is regenerated on the addition of hydrochloric acid. The solution in sodium carbonate is brownish-mauve ; that in aqueous sodium hydroxide is reddish-brown and remains so on boiling.

p-*Acetoxypropiophenone*.—This *substance* was prepared in order to attempt its conversion into an α-diketone. A mixture of *p*-hydroxypropiophenone (10 g.) and acetic anhydride (50 c.c.)

* A specimen recrystallised by slow evaporation of a solution in 6% alcoholic hydrogen chloride.

was refluxed for 4 hours; the product, isolated in the known manner, formed long needles, m. p. 59°, from aqueous alcohol (Found: C, 68·8; H, 6·2. $C_{11}H_{12}O_3$ requires C, 68·8; H, 6·3%).

The authors thank the Department of Scientific and Industrial Research for a Senior Research award (A. D. A.) and are also grateful for research grants made by Imperial Chemical Industries Ltd. and by the Government Grants Committee of the Royal Society. The same acknowledgments apply to Part III of this series.

Dyson Perrins Laboratory, Oxford University. [*Received, January 14th,* 1937.]

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99. *A Synthesis of Dihydrocarbostyril and Homodihydrocarbostyril by Ring Enlargement and a Synthesis of Tetrahydroquinoline.*

By Lindsay H. Briggs and Gordon C. De Ath.

Schmidt (*Ber.*, 1924, **57**, 704) has found that the action of hydrazoic acid on *cyclo*hexanone in the presence of concentrated sulphuric acid yields ε-leucine lactam by the introduction of an imino-group next to the carbonyl group with consequent ring enlargement. The reaction has now been extended to cyclic ketones attached to the benzene nucleus, *viz.*, α-hydrindone and α-tetralone. The former gives dihydrocarbostyril, m. p. 163°, in 68% yield, but none of the isomeric dihydro*iso*carbostyril, m. p. 71°. 5 : 6-Methylenedioxy-1-hydrindone, however, failed to react with hydrazoic acid in the presence of concentrated sulphuric acid, syrupy phosphoric acid or acetic anhydride, owing doubtless to the decreased carbonyl activity produced by electromeric effect of the methylenedioxy-group. α-Tetralone likewise yielded homodihydrocarbostyril, m. p. 141°, in 70% yield. Schroeter and co-workers (*Ber.*, 1930, **63**, 1308) obtained homodihydrocarbostyril also from α-tetralone by a Beckmann transformation of the oxime, using *p*-toluenesulphonyl chloride. By hydrolysis of homodihydrocarbostyril, γ-*o*-aminophenylbutyric acid was obtained, which by further treatment with hydrazoic acid and concentrated sulphuric acid gave γ-*o*-aminophenylpropylamine in 44% yield. The hydrochloride of the latter on dry distillation at atmospheric pressure gave a 50% yield of tetrahydroquinoline (cf. Ladenburg, *Ber.*, 1885, **18**, 3100; Helfer, *Helv. Chim. Acta*, 1923, **6**, 785).

In conformity with the position of the entering imino-group into α-hydrindone and α-tetralone, acetophenone on treatment with hydrazoic acid and concentrated sulphuric acid produces a 77% yield of acetanilide, no benzomethylamide being isolated.

Experimental.

Dihydrocarbostyril.—A mixture of α-hydrindone (2 g.; 1 mol.) in benzene (20 c.c.) and concentrated sulphuric acid (4 c.c.) was stirred at 40°, and a 5% solution of hydrazoic acid (1·5 mols.) in benzene gradually added. When reaction had ceased, the sulphuric acid layer was poured into water, precipitating a whitish solid, the quantity of which was increased by neutralisation of the acid with ammonia; yield, 1·52 g. (68%). By a single crystallisation from alcohol (charcoal) pure dihydrocarbostyril was obtained, m. p. 163°; Kipping (*J.*, 1894, **65**, 480) records m. p. 163°. From the benzene layer a very small amount of dihydrocarbostyril was obtained but no dihydro*iso*carbostyril.

Homodihydrocarbostyril.—A solution of α-tetralone (20 g.; 1 mol.) and hydrazoic acid (1·25 mols.) in chloroform (140 c.c.) was stirred at 40°, and concentrated sulphuric acid (36 c.c.; 5 mols.) gradually added (1 hour). The acid layer was poured into water (900 c.c.), and the creamy solid, homodihydrocarbostyril, crystallised from a large volume of hot water; m. p. 141°, yield 15·5 g. (70%). Von Braun (*Ber.*, 1907, **40**, 1843) and Schroeter and co-workers (*loc. cit.*) record m. p. 139—140°. The acid filtrate on neutralisation yielded a further small quantity of the same product.

Homodihydrocarbostyril (14 g.) was hydrolysed almost quantitatively into the hydrochloride of γ-*o*-aminophenylbutyric acid, m. p. 201° (von Braun, *loc. cit.*), by heating with concentrated hydrochloric acid (175 c.c.). The free acid, m. p. 125°, was obtained (91% yield) by treating a solution of the hydrochloride in the minimum amount of water with a saturated aqueous solution of sodium acetate. Schroeter *et al.* (*loc. cit.*) give m. p. 125—126°.

γ-o-Aminophenylpropylamine.—To a solution of γ-*o*-aminophenylbutyric acid (15 g.; 1 mol.) and hydrazoic acid (1·25 mols.) in chloroform (110 c.c.) at 40° was gradually added concentrated sulphuric acid (24 c.c.; 5 mols.). Reaction was less vigorous than in the previous cases and a further amount of concentrated sulphuric acid (10 c.c.; 2 mols.) was added, and the reaction allowed to proceed for 3·5 hours. The acid layer was poured into water (450 c.c.) and neutralised with concentrated sodium hydroxide solution. The mixture gave to ether a light yellow oil, b. p. 139—140°/19 mm., in 44% yield. Although the b. p. does not agree with that of γ-*o*-aminophenylpropylamine recorded by Kanevska, 165°/16 mm. (*J. pr. Chem.*, 1929, **124**, 33), the m. p.'s of the dibenzoyl derivative, m. p. 157—158° (from alcohol), and the dihydrochloride, m. p. 231—232°, prepared in dry ethereal solution by passage of hydrogen chloride, show good agreement with those of Kanevska's preparations, m. p. 158—159° and m. p. 228—230° respectively.

Since γ-phenylpropylamine belongs to the type of sympathomimetic amines (cf. Barger and Dale, *J. Physiol.*, 1910, **41**, 19; Hartung and Munch, *J. Amer. Chem. Soc.*, 1931, **53**, 1875), a sample of the hydrochloride was submitted for physiological tests. We are indebted for these tests to Dr. M. Bell, Otago University, who has reported that small doses, injected intravenously, produce a slight rise, followed rapidly by a slight temporary fall, of blood pressure.

Tetrahydroquinoline.—γ-*o*-Aminophenylpropylamine dihydrochloride (3·5 g.) was rapidly heated in a small retort. White fumes (ammonium chloride), a brown oil, and a reddish-brown solid were the products of distillation. The distillate was boiled with sodium hydroxide solution to remove ammonia and cooled. The residue gave to ether a colourless oil, b. p. 139—141°/35 mm., in 50% yield, identified as tetrahydroquinoline by means of the benzoyl derivative, m. p. 74—75° (lit. m. p. 75°), and the hydrochloride, prepared as in the previous case, m. p. 180° (lit. m. p. 180—181°).

Acetanilide.—Acetophenone (5 g.), treated similarly to α-hydrindone above, gave 4·3 g. (77% yield) of acetanilide.

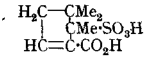
Auckland University College, New Zealand. [*Received, January 11th*, 1937.]

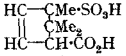
100. *The Constitution of Sulphocamphylic Acid.*

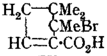
By J. R. Lewis and J. L. Simonsen.

Sulphocamphylic acid, first prepared by Walter (*Ann. Chim.*, 1843, **9**, 177) by the action of sulphuric acid on camphoric acid, was investigated subsequently by Kachler (*Annalen*, 1873, **169**, 179), Damsky (*Ber.*, 1887, **20**, 2959), Koenigs and Hoerlin (*ibid.*, 1893, **26**, 812, 2045), Koenigs and Meyer (*ibid.*, 1894, **27**, 3466), and Perkin, jun. (J., 1898, **73**, 799; 1903, **83**, 835).

As the outcome of his detailed studies of the reactions of the sulphonic acid, which he prepared also by the action of sulphuric acid on *iso*lauronolic acid, Perkin suggested that it was most probably represented by (I): later, Aschan ("Chemie der Alicyklischer Verbindungen," p. 572), without adducing any fresh experimental evidence, advanced the alternative formula (II) as being more in accord with its formation from camphoric acid.


(I.)


(II.)


(III.)

Although the formation of α-camphylic acid (dehydro-α-campholytic acid) on alkali fusion would be explained readily by (II), its conversion into β-camphylic acid (dehydro*iso*lauronolic acid) and into *iso*lauronolic acid are more in accord with (I). Neither formulation, however, accounts for the observation recorded by Koenigs and Hoerlin (*loc. cit.*, p. 2045) that the so-called sulphopimelic acid, $C_7H_{12}O_7S$, prepared by Kachler (*loc. cit.*, p. 181) by the oxidation of sulphocamphylic acid with nitric acid, decomposed on heating at 160—170° to give sulphur dioxide and terebic acid.

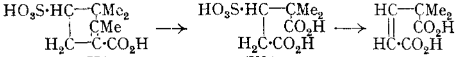
It was shown by Perkin (*loc. cit.*, p. 827) that when sulphocamphylic acid bromide was heated at 155° it gave an unsaturated bromo-acid, bromodihydro-β-camphylic acid, $C_9H_{13}O_2Br$, to which he assigned the structure (III). Oxidation of this acid with ozone has

now been found to give a liquid bromoketo-acid (*semicarbazone*, m. p. 190°), which on further oxidation with sodium hypobromite yields bromoform and *trans*-αα-dimethylglutaconic acid, elimination of hydrogen bromide accompanying the oxidation of the acyl group. The degradation to αα-dimethylglutaconic acid can only be explained if the bromo-acid is represented by either (IV) or (V); the bromoketo-acid would then be either (VI) or (VII).

(IV.) (VI.) (V.) (VII.)

The structure (V), 5-bromo-2 : 3 : 3-trimethyl-Δ^1-*cyclo*pentene-1-carboxylic acid, has, however, been assigned already to *isob*romodihydro-β-camphylic acid, which gives on ozonolysis, followed by oxidation with sodium hypobromite, *as*-dimethylsuccinic acid (Lewis and Simonsen, J., 1936, 735). It follows, therefore, that bromodihydro-β-camphylic acid must be 4-bromo-2 : 3 : 3-trimethyl-Δ^1-*cyclo*pentene-1-carboxylic acid (IV) and the bromoketo-acid must be (VI), the formulation of the latter as a β-bromo-acid accounting for the facile loss of hydrogen bromide in the presence of alkali.

These results suggested that sulphocamphylic acid must be 4-sulpho-2 : 3 : 3-trimethyl-Δ^1-*cyclo*pentene-1-carboxylic acid (VIII), a structure in accord with its conversion by alkali into α- and β-camphylic acids, but still irreconcilable with its degradation to terebic acid. We have therefore re-examined the oxidation of sulphocamphylic acid with nitric acid under the conditions used by Koenigs and his collaborators. We can confirm the formation of dimethylmalonic and oxalic acids, but we find that the so-called sulphopimelic acid (or sulpho*iso*propylsuccinic acid) gives on pyrolysis, not terebic acid, but a mixture of *cis*- and *trans*-αα-dimethylglutaconic acids (X). It follows, therefore, that sulphopimelic acid must be β-*sulpho-αα-dimethylglutaric acid* (IX), the reactions proceeding in accordance with the following scheme:



(VIII.) (IX.) (X.)

The recognition of sulphocamphylic acid as a sulpho*iso*lauronolic acid shows that the sulphonation of *iso*lauronolic acid proceeds without molecular rearrangement and it must be assumed that the primary action of sulphuric acid on camphoric acid is to give α-campholytic acid, which, as is well known, isomerises in the presence of mineral acids to *iso*lauronolic acid.

An attempt was made to confirm the structure assigned to sulphocamphylic acid by the ozonolysis of the acid itself and of its methyl ester. From the latter a stable *ozonide*, m. p. 83—85°, was obtained, but this ozonide and that obtained from the acid gave on decomposition viscid oils from which no crystalline derivatives could be prepared. The presence of an acyl group was, however, proved by the formation of bromoform on oxidation with sodium hypobromite. When the oil from the decomposition of the ozonide of sulphocamphylic acid was heated at 130—140°, it gave an unsaturated dibasic *acid*, $C_{16}H_{20}O_4$, m. p. 145—147°. This acid is possibly related to the diketo-acid, dicampherylic acid, $C_{18}H_{20}O_6$, obtained by Perkin by the oxidation of sulphocamphylic acid with potassium permanganate.

Experimental.

4-*Bromo*-2 : 3 : 3-*trimethyl*-Δ^1-cyclo*pentene*-1-*carboxylic Acid*.—The following modification of Perkin's method (*loc. cit.*, p. 827) was found convenient. Dry sulphocamphylic acid bromide (4 g.), heated in xylene (20 c.c.) at 125—135°, slowly dissolved, sulphur dioxide being evolved. If this temperature was exceeded, the yield was much diminished. After evolution of gas had ceased (2 hours), the solution was filtered from a little carbonaceous matter, and the xylene removed in steam, in which the bromo-acid was only slowly volatile. The bromo-acid (3 g.), which separated from the cooled aqueous solution, was recrystallised from dilute formic acid and then had m. p. 128—129°.

Oxidation of 4-*Bromo*-2 : 3 : 3-*trimethyl*-Δ^1-cyclo*pentene*-1-*carboxylic Acid*.—The acid (1 g.) in ethyl acetate (15 c.c.) was oxidised with ozone at 0°; formaldehyde was not detected in the issuing gases. After removal of the solvent under diminished pressure, the ozonide was decomposed by warming with water and the heavy oil which separated was extracted with ether. Removal of the solvent gave an oil, the *semicarbazone* of which separated from dilute acetic acid in plates, m. p. 190° (Found: C, 37·0; H, 5·6; N, 14·2; Br, 26·7. $C_9H_{16}O_3N_3Br$ requires C, 36·7; H, 5·4; N, 14·3; Br, 27·2%).

The bromoketo-acid (1·5 g.) was dissolved in dilute sodium carbonate solution and treated with an excess of sodium hypobromite at 0°; bromoform separated immediately. After 1 hour the bromoform was removed, the excess of hypobromite destroyed by sulphur dioxide, and the solution acidified and repeatedly extracted with ether. Evaporation of the solvent gave an oil, which crystallised on trituration with hydrochloric acid. The solid, recrystallised from hot water, formed leaflets, m. p. 169—171° alone and in admixture with *trans*-αα-dimethylglutaconic acid (Found: C, 53·4; H, 6·6. Calc. for $C_7H_{10}O_4$: C, 53·2; H, 6·3%).

Oxidation of Sulphocamphylic Acid.—The acid (6 g.), suspended in ethyl acetate (50 c.c.) at 0°, dissolved when ozone was passed in. After removal of the solvent the ozonide was suspended in water (10 c.c.), a clear solution being obtained on gentle warming. This gave on evaporation a viscid oil, which contained free sulphuric acid and gave with sodium hypobromite a copious precipitate of bromoform; attempts to prepare crystalline derivatives were unsuccessful. When the oil (2 g.) was heated at 130—140° for 3·5 hours, a gum was obtained, which dissolved in hot water (5 c.c.); the filtered solution on cooling deposited a brown solid. The *acid* crystallised from water (charcoal) in needles, m. p. 145—147° [Found: C, 69·3; H, 7·7; *M*, 265 (Rast), 276 (titration). $C_{16}H_{20}O_4$ requires C, 69·6; H, 7·3%; *M*, 276]. The acid was unstable to potassium permanganate in alkaline solution, but it was not oxidised by percamphoric acid. Catalytic hydrogenation in alcoholic solution with a palladium catalyst was slow and indicated the presence of three ethylenic linkages.

Ozonolysis of methyl sulphocamphylate (1 g.) in carbon tetrachloride (15 c.c.) at 0° gave an oil, from which, after warming with water for 30 minutes, ether extracted an *ozonide* crystallising from methyl alcohol in cubes, m. p. 83—85° (Found: C, 42·4; H, 5·8; S, 10·3. $C_{11}H_{18}O_8S$ requires C, 42·6; H, 5·8; S, 10·4%). Prolonged digestion of the ozonide with water gave a homogeneous solution, from which no crystalline products could be separated.

Pyrolysis of β-*Sulpho*-αα-*dimethylglutaric Acid*.—The acid, prepared as described by Koenigs and Hoerlin (*loc. cit.*), was heated under diminished pressure at 160—170°; sulphur dioxide was evolved and a small quantity of a crystalline solid (*A*) distilled. The brown crystalline residue in the distilling flask was dissolved in sodium carbonate solution, filtered from carbonaceous matter, and acidified. The acid, which separated, crystallised from water in leaflets, m. p. 170—171° alone and in admixture with *trans*-αα-dimethylglutaconic acid (Found: C, 53·0; H, 6·6; *M*, 162. Calc.: C, 53·2; H, 6·3%; *M*, 158). The acid (*A*), crystallised from hydrochloric acid and then from benzene, had m. p. 131° and was probably *cis*-αα-dimethylglutaconic acid, for which Perkin and Smith (J., 1903, **83**, 16) record m. p. 135° (Found: C, 53·2; H, 6·3%; *M*, 161).

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University College of North Wales, Bangor. [*Received, February 2nd*, 1937.]

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101. *Salt Hydrates and Deuterates. Part I. The Dissociation Pressures of Certain Deuterates.*

By James Bell.

It has been pointed out by Day, Hughes, Ingold, and Wilson (J., 1934, 1593), considering Werner's conception of the structure of salt hydrates and the relative stabilities of hydrogen and deuterium bonds, that salts in which the water molecules are regarded as linked to the cation should show a preference for light water when crystallised from a mixture of light and heavy water. Conversely, in the case of anion-hydration, a relative preference for heavy water should be expected. These investigators crystallised a number of salts from a

dilute solution of deuterium oxide, but obtained no evidence of any preference for light or heavy water, and concluded that any structure arising out of hydration must be of a loose character.

It is probable, however, that a study of the properties of the pure deuterates and their comparison with those of the corresponding hydrates may furnish evidence applicable to the question of the structure of the hydrated salts. In the course of an extended investigation of this type, the dissociation pressures of certain deuterates have been measured over a range of temperature and compared with those of the corresponding hydrates. This communication, which is of a preliminary nature, contains the results obtained in a study of some sulphates and chlorides and hydrated sodium bromide. The transition points of the deuterates also have been determined where possible.

Experimental.

The dissociation pressures were measured by the tensimetric method, a modification of the Bremer–Frowein tensimeter being used. The tensimeters were immersed in a gas-heated thermostat, accurate to $\pm$ 0·05°, and in most cases 24 hours were allowed to elapse before the reading of the pressure was made. In other experiments a longer interval was necessary for the establishment of equilibrium. Mercury was used as the manometric liquid. The heavy water used in these experiments was the product of the Norsk Hydroelektrisk Kvaelstofaktieselskab and contained 99·95% of deuterium oxide.

Table I shows the results for the dissociation pressures of copper sulphate pentadeuterate, sodium sulphate decadeuterate, magnesium sulphate heptadeuterate, strontium chloride hexadeuterate, cobalt chloride hexadeuterate, nickel chloride hexadeuterate, and sodium bromide dideuterate. Values are also included for the dissociation pressures of strontium chloride hexahydrate, as there is considerable diversity in the results previously recorded, and for sodium bromide dihydrate, which does not appear to have been investigated over a range of temperature.

Transition points were determined from the graphs of log p against $10^6/T$, p being in mm. of mercury.

Table I.

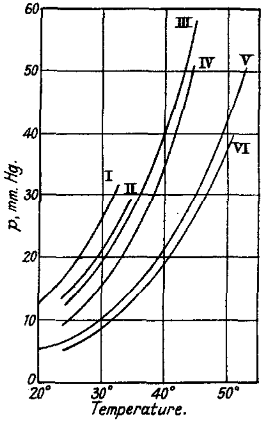
t.	*p.*	*t.*	*p.*	*t.*	*p.*	*t.*	*p.*
$CuSO_4,5D_2O$.		$MgSO_4,7D_2O$.		$SrCl_2,6D_2O$.		$NaBr,2D_2O$.	
25°	6·5	25°	9·9	25°	6·9	20°	4·25
30	9·3	30	15·6	30	10·7	25	6·9
35	13·7	34·6	22·7	35	14·9	30	10·45
39	19·4	40·5	36·6	40	20·4	35	15·1
		44·9	50·0			40	21·6
$Na_2SO_4,10D_2O$.		49·4	67·1	$SrCl_2,6H_2O$.		44·5	30·2
25	14·5	51·5	74·5	25	7·3	49·8	44·8
30	21·0	53·2	81·0	30	11·0	51·3	45·0
33	26·2			35·2	15·7	53·8	51·4
34	28·1	$CoCl_2,6D_2O$.		40	22·0		
35	30·0	25	5·8			$NaBr,2H_2O$.	
36	31·9	30	9·1	$NiCl_2,6D_2O$.		20	4·9
38	35·7	34·9	13·1	24·8	7·8	25	7·5
40	39·9	40	18·7	30	12·2	30	11·3
		45·1	26·7	34·3	17·4	35	16·4
		49·9	37·0	38	21·8	40	22·9
		54·5	48·5	42·3	26·4		
		56·6	54·5	46·2	30·9		

Discussion of Results.—The only deuterate for which values of the dissociation pressure have been previously recorded is copper sulphate pentadeuterate, Schacherl (*J. Phys. Radium*, **1935**, **6**, 439; *Nature*, 1936, **138**, 406) and Partington and Stratton (*ibid.*, **137**, 1075) having investigated the change, $CuSO_4,5D_2O \rightleftharpoons CuSO_4,3D_2O + 2D_2O$. The results for the dissociation pressure in the present series of measurements are in agreement with the values reported by these workers.

Although it is impossible to make any generalisations until the dissociation pressures of many more deuterates have been examined, the results already obtained are of interest. The mean values for the ratio of the dissociation pressure of the deuterate to that of the corresponding hydrate, over a range of temperature in which these pressures were measured, are as follows:

	$CuSO_4$.	Na_2SO_4.	$MgSO_4$.	$SrCl_2$.	$NiCl_2$.	$CoCl_2$.	NaBr.
p_{D_2O}/p_{H_2O}	0·82	0·81	0·82	0·95	0·82	0·87	0·90

The relatively lower value of this ratio for the first three salts is well defined. In the figure, for example, are shown the dissociation-pressure curves for the hydrate and deuterate of three of the salts, sodium sulphate, magnesium sulphate, and cobalt chloride. The



I, $Na_2SO_4,10H_2O$; II, $Na_2SO_4,10D_2O$; III, $MgSO_4 7H_2O$; IV, $MgSO_4,7D_2O$; V, $CoCl_2,6H_2O$; VI, $CoCl_2,6D_2O$.

TABLE II.

$Na_2SO_4,10H_2O \longrightarrow Na_2SO_4$	32·4°
$Na_2SO_4,10D_2O \longrightarrow Na_2SO_4$	34·48 *
	34·5 †
$CoCl_2,6H_2O \longrightarrow CoCl_2,2H_2O$	52·25
$CoCl_2,6D_2O \longrightarrow CoCl_2,2D_2O$	51·1
$SrCl_2,6H_2O \longrightarrow SrCl_2,2H_2O$	61·3
$SrCl_2,6D_2O \longrightarrow SrCl_2,2D_2O$	56·5 ‡
$NiCl_2,6H_2O \longrightarrow NiCl_2,4H_2O$	36·25
$NiCl_2,6D_2O \longrightarrow NiCl_2,4D_2O$	35·9
$NaBr,2H_2O \longrightarrow NaBr$	50·7
$NaBr,2D_2O \longrightarrow NaBr$	47·7
$MgSO_4,7H_2O \longrightarrow MgSO_4,6H_2O$	48·4
$MgSO_4,7D_2O \longrightarrow MgSO_4,6D_2O$	46·8

* Taylor, *J. Amer. Chem. Soc.*, 1934, **56**, 2643.
† Present work.
‡ Miles, Shearman, and Menzies, *Nature*, 1936, **138**, 121.

differences in pressure are clearly illustrated. For nickel chloride the ratio rises steadily from 0·75 at 25° to 0·88 at 35°, so the mean figure is probably of little value.

The ratios of the heats of dissociation have been determined from the relative slopes of the curves of log p against $1/T$, and the following values found :

	$CuSO_4$.	Na_2SO_4.	$MgSO_4$.	$SrCl_2$.	$NiCl_2$.	$CoCl_2$.	NaBr.
Q_{D_2O}/Q_{H_2O}	1·09	1·08	1·09	0·99	1·31	1·05	1·03

It is proposed to study the relative dissociation pressures of the different hydrates and deuterates of the same salt, where this is possible, *e.g.*, the hepta- and hexa-hydrates and -deuterates of magnesium sulphate, for such a complete examination is obviously necessary before any conclusions regarding the structure of hydrates can be derived.

Table II shows the transition points of the deuterates where these have been determined, together with the accepted values for the corresponding hydrate transitions.

Sodium sulphate decadeuterate is the only example, so far, of a deuterate which has a higher transition point than the corresponding hydrate.

I desire to thank Imperial Chemical Industries, Ltd., for a gift of heavy water, the Chemical Society for a grant from the Research Fund, and the Carnegie Trust for the award of a Teaching Fellowship.

THE UNIVERSITY, GLASGOW. [*Received, January 30th*, 1937.]

102. *Combination of Fatty Acids with Nitrogen Bases. Part III. Molecular Weight, Surface Tensions, Viscosities, and Conductivities in Benzene of the System : Piperidine–Propionic Acid.*

By E. B. R. Prideaux and R. N. Coleman.

If the piperidine salts of the lower fatty acids are largely undissociated in the pure state, as suggested in Part II (this vol., p. 4), it might be expected that they would have this character also in the associating solvent benzene; and therefore the physical properties of various mixtures of acid and base in benzene would bear a general resemblance to those of corresponding mixtures without solvent. Solutions containing less than 25% of the salt are no better conductors than benzene itself (as is shown below), so the properties observed should be due to molecules alone, including polymers.

The experiments already carried out in the absence of solvent were repeated in benzene solution. For this purpose, the system, piperidine–propionic acid, was chosen as being typical of the series. The molecular complexity of piperidinium propionate in benzene was determined cryoscopically; the densities and surface tensions of solutions containing various proportions of piperidine and propionic acid were measured. The sum of the weights of acid and base in these experiments was always 25% of the whole.

The conductivities and viscosities of piperidinium propionate in benzene solution were observed over the range 0—100% of salt, and from these results the variation of the product $\Lambda\eta$ with concentration was deduced.

Molecular Complexity in Benzene.—Compounds dissolve in benzene either as single molecules or as polymers. Association is found even in simple non-polar, or very feebly polar, compounds, but is still more pronounced in substances of a polar character such as benzoic acid. Such behaviour was observed in a comprehensive investigation of the association of a large number of organic substances, representing many different types of compounds, in benzene and other solvents (Meisenheimer and Dorner, *Annalen*, 1930, **482**, 130); it was, further, concluded that as a general rule the degree of association increases linearly with the concentration of the solution. The relation of molecular association to electrolytic dissociation was studied by Turner (J., 1911, **99**, 880), who showed that the halogen salts of organic bases exhibited very pronounced association in chloroform, the degree of association in dilute solutions being much greater than that which other substances, *e.g.*, organic acids, show in concentrated solutions. It was concluded that substances which are associated are either electrolytes or conducting media, and that molecular association in non-ionising solvents is complementary to electrolytic dissociation in water; and it was pointed out that the rate of increase of association is generally linear for such substances, and that the degree of association is dependent on two factors, one for the acid and one for the base. It will be seen that these conclusions apply to the salt now under consideration.

The usual technique of the Beckmann cryoscopic method was followed, the liquid salt being introduced into weighed, dry benzene. It was necessary to employ a stirrer working through a mercury seal, for otherwise the salt absorbed moisture which, even in quite minute amounts, gave a turbid suspension, evidently due to the separation of an aqueous phase. The distribution ratio of the salt between water (with which it is completely miscible) and benzene is therefore very high. The solid benzene which separated was free from the salt.

The molecular weights were calculated in the usual way, the results being best summarised by the equation $\alpha = 0{\cdot}0112C + 1{\cdot}96$, in which α is the molecular complexity (M, obs./M, calc.), and C is the concentration (% by wt.) of the solution. Observations were carried out over the range $C = 5$—25. The salt exists in benzene, therefore, largely as double molecules, and α increases linearly with concentration. The molecular complexity is not, however, quite as great as is that of most of the halogen salts studied by Turner (*loc. cit.*); *e.g.*, for tetra- and for di-ethylammonium chloride, $\alpha = 3{\cdot}90$—$5{\cdot}90$ and $2{\cdot}51$—$3{\cdot}37$ respectively. The lower association of the piperidine salt in benzene would, according to the above theory, be connected with the relatively lower dissociation in the pure state.

Densities and Surface Tensions.—These properties should be but little affected by the

presence of benzene, and should therefore be calculable by the additive law. All mixtures contained 75% by weight of benzene, and a total of 25% of piperidine and propionic acid in various proportions as solute. Mixtures were prepared from stock solutions containing 25% of acid and base severally. Densities were determined by density bottle, and surface tensions by the double capillary-tube method, in a thermostat at 25·0° as already described (Part I, J., 1936, 1346). Precautions were taken against evaporation of benzene and absorption of moisture. Results are given in Table I, and represented graphically in Figs. 1 and 2.

TABLE I.

Acid in solute, wt. %.	$d^{25°}_{4°}$.	*d*, calc.	γ.	γ, calc.	Acid in solute, wt. %.	$d^{25°}_{4°}$.	*d*, calc.	γ.	γ, calc.
0·0	0·8702	0·8716	28·48	28·46	64·9	0·9070	0·9119	28·72	29·26
14·5	0·8814	0·8837	28·56	28·65	81·1	0·9036	0·9099	28·24	28·41
28·4	0·8919	0·8953	28·79	29·12	100·0	0·8952	0·9005	27·14	27·51
46·5	0·9037	0·9102	29·00	30·14					

Densities. The densities of the solutions first increase linearly with increasing proportion of acid, then pass through a rather flat maximum, and finally fall along a curve to the

FIG. 1.

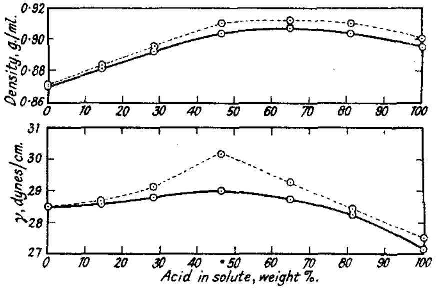


FIG. 2.

value for 25% of propionic acid in benzene. This behaviour is closely similar to that observed in the benzene-free system. In both cases the maximum density is not shown by the salt (which contains 46·5% of acid) but by a mixture of piperidine and propionic acid containing 65% of acid. If solutions of the acid–base mixtures in benzene obeyed the mixture law, a curve indicated by the broken line in Fig. 1 would be obtained, this being calculated as follows: Density of solution $= 0{\cdot}75d_B + 0{\cdot}25d_X$, where d_B is the density of benzene and d_X that of the benzene-free system interpolated from the previous results (Part I). This curve is seen to lie only slightly above that actually obtained, agreement being closer on the basic side of the curve, while on the acid side there is a small, fairly constant difference of 0·005—0·006. It may therefore be concluded that the mixture law is approximately obeyed between the densities of benzene and those of the system piperidine–propionic acid.

Surface tensions. It is evident that the general form of the surface tension curve due to different degrees of salt formation in the unsolvated system is broadly repeated in benzene solution. By assuming the mixture law, values of γ for the solutions, represented by the broken line on the graph, may be calculated by means of interpolations from the previous data of the benzene-free system, together with the surface tension of benzene itself. The values of γ so calculated are higher than those observed. Hence it is seen that the surface tensions of the pure system are lowered by the presence of benzene to a considerably greater

extent than is accounted for by the additive effect due to the liquid of lower surface tension, *viz.*, benzene. The effect is, however, not uniform in different parts of the curve. Piperidine has a somewhat higher surface tension than benzene, and the surface tension of a 25% solution of the former is practically that required by the mixture law. As the acid content increases, the experimental curve departs further from the calculated, the difference reaching a maximum of 1·1 dynes/cm. at the salt concentration. Further addition of acid causes the curves to approach, and finally the pure acid in benzene has a value of γ a little below that required by the mixture law. Since propionic acid is capillary-active, it may be expected that this liquid will be concentrated in the surface, and will thus decrease γ. On the other hand, although piperidine may be capillary-active to most solvents, it has a higher surface tension than benzene itself, so there will be no tendency towards surface adsorption. The fact that the surface tension of the benzene solution of the salt itself is less than the calculated value cannot be accounted for by the concentration of the salt in the surface of the benzene, since the salt has a higher surface tension than benzene. Such an explanation would rather require negative adsorption, or a concentration of benzene molecules in the surface. In Part I, incomplete combination was suggested as an explanation of the low surface tensions of the piperidine salts of the fatty acids as compared with the values required for theoretical parachors. Similarly, it seems probable that, in benzene solution, enough free acid is produced by dissociation to permit surface adsorption, thus lowering the values of γ. This effect disappears in solutions containing sufficient excess of piperidine to suppress dissociation. The position of the maximum is the same as in the benzene-free system, *i.e.*, at 50 mols.%. The evolution of heat observed on mixing the constituents in benzene solution being taken into consideration, this maximum may be likewise attributed to the formation of a salt pair, or polymer, which is inactive, from capillary-active constituents.

The parachor of piperidinium propionate in benzene solution calculated from the mixture law according to the method of Hammick and Andrew (J., 1929, 754) is 376·6, while that of the salt free from solvent is 382·6. It has already been shown that the latter is below that calculated from the atomic values, and also below the sum of the parachors of free acid and base. Therefore the factors which cause this deviation are operative also in benzene solution. Evidence from the cryoscopic data indicates that a partial explanation is to be found in the association of the salt in solution.

Conductivities and Viscosities in Benzene.—Previous data for the conductivity of salts in benzene are limited, since, as a rule, salts are not sufficiently soluble to give conducting solutions. Piperidinium propionate, however, is miscible with benzene in all proportions. Cady and Baldwin (*J. Amer. Chem. Soc.*, 1921, **43**, 646), studying reactions in benzene, found that copper melissate, lead stearate, and similar salts in this solvent showed some conductivity, which increased on passing in dry hydrogen chloride. Silver perchlorate is fairly soluble in benzene, but gives non-conducting solutions (Hill, *ibid.*, p. 254). The thiohydrate of aluminium bromide, $AlBr_3,H_2S$, is soluble in benzene, and the specific conductivity over the range 20—54% of salt has been shown by Jakubsohn (*Z. physikal. Chem.*, 1925, **118**, 31) to rise to $3{\cdot}54 \times 10^{-4}$ ohm^{-1} for the most concentrated solution.

Specific conductivities of piperidinium propionate in benzene were determined at 25·0° by the method already described. Finite values were obtained in solutions containing more than 30% of the salt. Densities in benzene (Table II) were found to give a nearly linear graph against the concentration. From these—by interpolation—molar conductivities were calculated, the results being included in Table III and shown in Fig. 3.

The maximum specific conductivity is observed at 72% of salt. The conductivities are of the same general order as those shown by the salt $AlBr_3,H_2S$ (see above) at corresponding concentrations. The maximum molar conductivity occurs at 66% of salt. It appears, therefore, that a mixture of the salt with a small quantity of benzene is a better conductor than the pure salt, in spite of the fact that benzene is a non-ionising solvent. Any increase of electrolytic dissociation would appear to be out of the question, since double molecules are already present in less concentrated solutions (see p. 462), and molecular complexity has been found to increase with increasing concentration. It is more probable that the relatively small proportion of free ions to which the conductivity of the pure salt is due is

TABLE II.

Salt, wt. %	100·0	87·1	69·2	58·3	48·6	34·0	0·0
d	1·0230	0·9998	0·9696	0·9535	0·9393	0·9187	0·8725
η	2·790	0·5697	0·1111	0·0549	0·0309	0·0164	0·0060

TABLE III.

Salt, wt. %.	$\kappa \times 10^4$.	Λ.	η.*	Λη.	Salt, wt. %.	$\kappa \times 10^4$.	Λ.	η.*	Λη.
100·0	5·47	0·0851	2·790	0·2374	48·2	4·21	0·1483	0·031	0·0045
85·2	9·00	0·1688	0·478	0·0807	34·5	0·52	0·0261	0·017	0·0004
71·3	9·66	0·2218	0·132	0·0293	20·6	0·00	0·0000	—	0·0000
60·6	8·02	0·2203	0·064	0·0141					

* Interpolated.

diminishing, although the mobility of the ions is increasing. The tendency towards a lower conductivity owing to the addition of a non-ionising solvent is at first more than counterbalanced by the increase due to greater mobility. The former factor soon begins

FIG. 3.

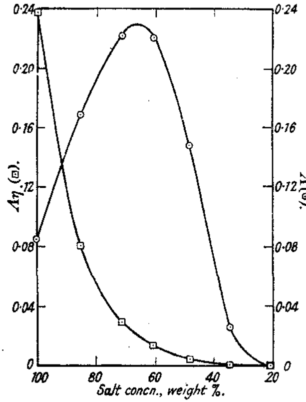
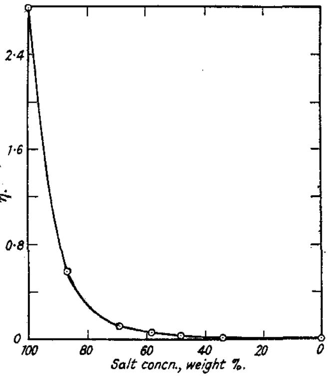


FIG. 4.



to predominate, however, and the curve falls steeply through 50% of salt to a negligible conductivity at 25%. The general behaviour is similar to the conductivity variations of the salt in excess of acid and of base already observed.

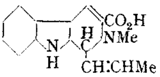
An examination of the variation of viscosity, η, with concentration shows that the increase in mobility may be largely, if not wholly, attributed to a rapid fall in viscosity on the addition of a relatively small quantity of benzene. Viscosity was determined as described in Part II, the usual precautions being taken. The results are included in Table II and shown by Fig. 4. The curve is seen to be approximately hyperbolic. Values were interpolated from this curve and included in Table III, whereby the product $\Lambda\eta$ was calculated. This is represented on Fig. 3, and is seen to fall steeply throughout with the addition of benzene. If this product is considered as representing the proportion of free ions, then the presence of the non-ionising solvent benzene has the effect of rapidly preventing the electrolytic dissociation of the salt.

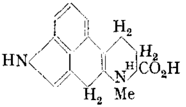
UNIVERSITY COLLEGE, NOTTINGHAM. [*Received, January 30th, 1937.*]

103. *Synthesis of Norharmancarboxylic Acid and its Bearing on the Constitution of Lysergic Acid.*

By Harold King and Eric T. Stiller.

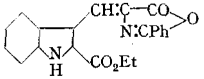
From the work of Smith and Timmis in this country and of Jacobs and Craig in the United States it is known that the chief alkaloids of ergot are substituted amides of lysergic acid, $C_{16}H_{16}O_2N_2$. The constitution of lysergic acid is still in doubt. Smith and Timmis (J., 1932, 764) emphasised the similarity between the colour reactions of ergine (lysergic acid amide) and those of indole or its derivatives. On phytochemical grounds, therefore, one might expect, for lysergic acid, a structure derived from tryptophan, and this received expression in the structure (I) put forward by Jacobs and Craig (*J. Biol. Chem.*, 1935, **111**, 455) on experimental grounds. The most recent structure (II) advanced by these

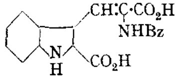
(I.) 

 (II.)

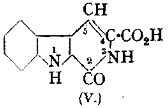
authors (*ibid.*, 1936, **115**, 227), based on further degradative work, can also be derived from tryptophan. These formulæ are partly based on drastic degradation methods applied to an admittedly sensitive molecule, coupled with elegant methods for the isolation of breakdown products, and one may entertain legitimate doubts of formulæ based on such evidence.

In the present communication an account is given of the synthesis of norharmancarboxylic acid, containing the nuclear structure of (I), for comparison with lysergic acid, and of some unusual intermediate products. An approach to this system seemed possible by applying the method developed for the synthesis of *iso*carbostyrils by Bain, Perkin, and Robinson (J., 1914, **105**, 2393) to 2-carbalkoxyindole-3-aldehydes. 2-Carbethoxyindole-3-aldehyde is readily available and on condensation with hippuric acid gave the azlactone, 2-phenyl-4-(2′-carbethoxyindolylidene)oxazolone (III) (Fischer and Pisbor, *Ber.*, 1923, **56**, 2317), a reactive substance which underwent many of the changes shown by Erlenmeyer (*Annalen*, 1893, **275**, 1) to be characteristic of this type of substance. On hydrolysis under the conditions described by Bain, Perkin, and Robinson, this azlactone

(III.) 

 (IV.)

gave *2-carboxyindole-3-(α-benzamido)acrylic acid* (IV) as the sole identifiable product. When, however, aqueous potassium hydroxide was replaced by 10% methyl-alcoholic potassium hydroxide, a mixture of products was obtained. During the hydrolysis, the potassium salt of *2-keto-2 : 3-dihydro-β-carboline-4-carboxylic acid* (V) crystallised. On concentration of the mother-liquors, dilution with water, and neutralisation, a substance, $C_{15}H_{16}O_4N_2$, separated to which, on the basis of the evidence given below, is ascribed the constitution (VI, R = Me), namely, *methyl 2-keto-2 : 3-dihydro-β-carboline-4-orthoformate*.



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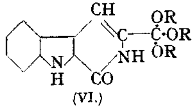
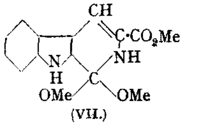


(VI.)

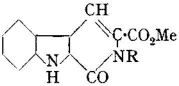


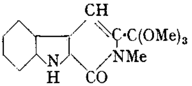
(VII.)

On acidification of the mother-liquors, the acrylic acid (IV), benzoic acid, and a small quantity of (V) were isolated in a pure condition and evidence for the presence

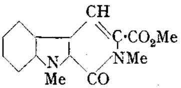
of 2-carboxyindolepyruvic acid (or a derivative) was found by the reaction with ketone reagents.

The orthoformic ester (VI) contains four oxygen atoms, three of which are attached to methyl. During the process of its formation the original ethoxy-group has been eliminated, for the same orthoformic ester was formed if 2-carbomethoxyindole-3-aldehyde was the starting point for the azlactone. In the hydrolytic process which has resulted in the production of the orthoformic ester, the benzoyl and ethyl groups have been eliminated but the oxygen atoms of the carbonyl groups in the original azlactone are retained. The three methoxy-groups must therefore be attached to these carbonyl groups, the only alternative structure being (VII). Of the structures (VI) and (VII), we prefer (VI), since (VII) is, we believe, without analogy among organic compounds. In favour of the structure (VI) may be quoted the observations that the orthoformate gave a purple-brown colour with ferric chloride and formed a potassium salt of phenolic type. On gentle hydrolysis with dilute acids it readily yielded a methyl ester, namely, *methyl* 2-*keto*-2 : 3-*dihydro*-β-*carboline*-4-*carboxylate* (VIII, R = H), a reaction characteristic of orthoformic esters (Skrabal and Ringer, *Monatsh.*, 1921, **42**, 9), and the stability to alkali under conditions

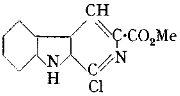
(VIII.) 

 (IX.)

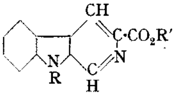
which brought about hydrolysis of the ester (VIII, R = H) speaks against the formula (VII). On methylation of the *potassium* derivative of the orthoformic ester with methyl iodide or of the orthoformic ester with diazomethane, methylation took place on the imide nitrogen atom with formation of *methyl* 2-*keto*-3-*methyl*-2 : 3-*dihydro*-β-*carboline*-4-*orthoformate* (IX). On acid hydrolysis this *N*-methylated orthoformate gave *methyl* 2-*keto*-3-*methyl*-2 : 3-*dihydro*-β-*carboline*-4-*carboxylate* (VIII, R = Me). If methylation of the orthoformate was carried out in acetone solution with methyl sulphate and potassium carbonate, *methyl* 2-*keto*-1 : 3-*dimethyl*-2 : 3-*dihydro*-β-*carboline*-4-*carboxylate* (X) was formed.



(X.)



(XI.)



(XII.)

By use of 10% ethyl-alcoholic potassium hydroxide for saponifying the original azlactone (III), the methyl orthoformate (VI, R = Me) was replaced by its *ethyl* homologue (VI, R = Et). The formation of these orthoformic esters and their transformations are not confined to substances derived from the indole nucleus, but are exactly paralleled by the reactions of the azlactone derived from methyl phthalaldehydate (see Stiller, following paper).

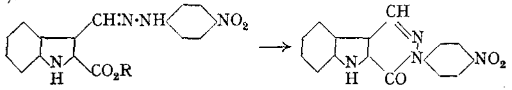
When the carboxycarbolone (V) was treated with 2 molecular proportions of phosphorus pentachloride in phosphorus oxychloride, and the crude products of the reaction separated by conversion into the methyl esters and fractionally crystallised, *methyl* 2-*chloro*-β-*carboline*-4-*carboxylate* (XI) was isolated as the main product. From the acidic mother-liquors a small quantity of the *dihydrochloride* of a *base*, $C_{25}H_{20}O_4N_4$, was obtained. This yielded on treatment with alcohol a colourless amorphous base which was almost insoluble in the usual solvents but could be crystallised from pyridine. On the available evidence we are unable to suggest a satisfactory structure for this substance, but as it contains two methoxy-groups and is dibasic, it must be formed by fusion of two molecules of the original carboxycarbolone with simultaneous reduction of the imide links (to account for the basic character) and loss of one carbon atom.

The chloro-carboline ester (XI) on alkaline hydrolysis gave 2-*chloro*-β-*carboline*-4-*carboxylic acid*. The halogen atom in these substances was firmly bound and could not

be removed catalytically, but on boiling the ester with hydriodic acid and red phosphorus a non-separable mixture was obtained containing the corresponding iodo-acid and its reduction product. When, however, the ester was reduced at 180° with hydriodic acid and red phosphorus, *norharmancarboxylic acid* (XII, R = R′ = H) was readily obtained. This acid, unlike the parent chloro-acid, showed a pronounced blue fluorescence in dilute acid solution and on decarboxylation gave norharman, characterised both as the base and as its picrate. The properties agreed with those recorded for norharman and its picrate by Kermack, Perkin, and Robinson (J., 1921, **119**, 1621). The methyl ester (XII, R = H, R′ = Me) was regenerated from norharmancarboxylic acid by boiling with methyl alcohol and sulphuric acid, but if diazomethane was used, methylation also took place on the indole nitrogen atom with formation of *methyl 1-methyl-β-carboline-4-carboxylate* (XII, R = R′ = Me).

Norharmancarboxylic acid, which may be looked upon as the parent substance of the structure (I) first proposed for lysergic acid, did not react significantly with indole reagents such as *p*-dimethylaminobenzaldehyde and glyoxylic acid, nor did its derivatives. A close comparison was consequently made of the colour reactions of ergometrine (α-alanolamide of lysergic acid) with these reagents and those of indole, 2-methylindole, tryptophan, and the four isomeric α- and β-methylbenzindoles prepared from α- and β-naphthylamines. The greatest similarity was found between the colour reactions of tryptophan and ergometrine, the latter being, however, much more reactive with the glyoxylic acid reagent. Next in order of resemblance came the indoles derived from β-naphthylamine. There can therefore be little doubt that lysergic acid does not contain a β-carboline skeleton, but must contain a more open indole-type of structure (compare Jacobs and Craig, *J. Biol. Chem.*, 1936, **113**, 767). The formation of a red picrate by ergometrine (Dudley, *Proc. Roy. Soc.*, 1935, *B*, **118**, 478) points in the same direction, since red picrates are formed from indoles which may be substituted in the α- or β-positions or on the nitrogen atom or even by an αβ-ring system such as carbazole, but not apparently by carbolines or analogous structures.

The starting materials in this investigation, 2-carbethoxy- and 2-carbomethoxy-indole-3-aldehydes, reacted with *p*-nitrophenylhydrazine with production of deeply coloured *p*-nitrophenylhydrazones (XIII), which passed smoothly under the influence of heat into the first representatives of a new ring system, *2-p-nitrophenylindolo(2′ : 3′ : 4 : 5)pyridaz-3-one* (XIV).

(XIII.)  (XIV.)

Experimental.

2-Carbalkoxyindole-3-aldehydes.—*o*-Nitrophenylpyruvic acid was prepared by the condensation of *o*-nitrotoluene and ethyl oxalate by the method of Reissert (*Ber.*, 1897, **30**, 1036). The reduction and ring closure to indole-2-carboxylic acid was effected by the method of Kermack, Perkin, and Robinson (J., 1921, **119**, 1625), by the action of ferrous sulphate on an ammoniacal solution of the acid. The methyl and the ethyl ester were then obtained in excellent yield by the method used by Fischer and Pisbor (*Ber.*, 1923, **56**, 2317) for the preparation of the ethyl ester.

2-Carbethoxyindole-3-aldehyde was prepared from ethyl indole-2-carboxylate following Boyd and Robson's (*Biochem. J.*, 1935, **29**, 555) use of Adams and Levine's (*J. Amer. Chem. Soc.*, 1923, **45**, 2373) modification of the Gatterman hydrogen cyanide method. *2-Carbomethoxyindole-3-aldehyde* was prepared by the same method, but its isolation was indirect. Methylindole-2-carboxylate in ethereal solution was treated with zinc cyanide and dry hydrogen chloride. The imino-chloride obtained was decomposed by boiling with water; but, unlike the carbethoxyindolealdehyde, the carbomethoxy-derivative could not be satisfactorily freed from unchanged ester by fractional crystallisation. The crude aldehyde (14 g.) was therefore dissolved in ethyl alcohol (7·5 c.c.) and treated on the water-bath with aniline (7·5 g.) for 15 minutes, a further quantity of alcohol (70 c.c.) added, and the solution boiled for 30 minutes.

When the red solution was cooled, *2-carbomethoxyindole-3-aldehyde anil* crystallised as a mass of yellow needles (12·75 g.). Recrystallised from alcohol, the anil had m. p. 163—164° (Found: C, 73·3; H, 4·9. $C_{17}H_{14}O_2N_2$ requires C, 73·3; H, 5·1%). The anil (12·5 g.) was decomposed by warming with dilute hydrochloric acid for an hour. The aldehyde (9·0 g.) was collected by filtration and on crystallisation from chloroform separated in colourless rectangular plates, m. p. 209—210° (Found: C, 64·8; H, 4·4. $C_{11}H_9O_3N$ requires C, 65·0; H, 4·5%).

2-Phenyl-4-(2'-carbethoxyindolylidene)oxazolone (III).—2-Carbethoxyindole-3-aldehyde (28 g.) was intimately mixed with finely powdered hippuric acid (35·2 g.) and anhydrous sodium acetate (12 g.) and suspended in acetic anhydride (160 c.c.). The mixture was heated on a boiling water-bath for 30 minutes; the solids gradually passed into solution and finally the liquid set to a mass of orange needles. When cold, the product was diluted with water, and the solids were collected and ground under sodium bicarbonate solution. The dried solid was further purified by refluxing twice with chloroform (800 c.c.), which removed unchanged aldehyde and other impurities. The azlactone (21 g.) was finally obtained as long, fine, matted, orange needles, m. p. 249—250° (Fischer and Pisbor, *loc. cit.*, give 242° with decomposition) (Found: C, 70·2; H, 4·6; N, 8·0. Calc.: C, 70·0; H, 4·4; N, 7·8%). The chloroform mother-liquors were evaporated to dryness, and the powdered residue re-treated with hippuric acid as described above, a further 15 g. of the azlactone thus being obtained.

2-Phenyl-4-(2'-carbomethoxyindolylidene)oxazolone.—This *azlactone* was prepared by the method described above for the ethyl homologue. The yield was similar and the product after crystallisation from glacial acetic acid had m. p. 253—254° (Found: C, 69·4; H, 4·0. $C_{20}H_{14}O_4N_2$ requires C, 69·4; H, 4·1%).

Aqueous Alkaline Hydrolysis of 2-Phenyl-4-(2'-carbethoxyindolylidene)oxazolone.—The azlactone (2 g.) was heated on the water-bath with 8% potassium hydroxide solution (27 c.c.). After 30 minutes a clear, deep red solution was obtained, which on acidification gave a yellowish-white precipitate. On crystallisation from absolute ethyl alcohol *2-carboxyindole-3-(α-benzamido)acrylic acid* (IV) separated in pale yellow, rectangular plates (1·7 g., m. p. 223—224° decomp.) containing one molecule of alcohol of crystallisation (Found for air-dried material: loss at 110°, 11·5; OEt, 10·6; equiv. by titration, 388. $C_{19}H_{14}O_5N_2,C_2H_5 \cdot OH$ requires loss, 11·6; OEt, 11·4%; equiv. 396. Found for dried material: C, 65·0; H, 4·0; N, 7·9; equiv., 356. $C_{19}H_{14}O_5N_2$ requires C, 65·1; H, 4·0; N, 8·0%; equiv., 350). This acid is very sparingly soluble in boiling water but moderately so in boiling glacial acetic acid and crystallises from the latter solvent in canary-yellow tablets, m. p. 233—234°, containing acetic acid of crystallisation which is tenaciously held.

Ethyl 2-Carbethoxyindole-3-(α-benzamido)acrylate.—The carbethoxy-azlactone (1·5 g.) was boiled under reflux with absolute ethyl alcohol (35 c.c.), and small amounts of anhydrous sodium carbonate added until complete solution had been effected; the colour changed from orange to pale yellow (5 minutes). The hot solution was filtered, and water added to the filtrate to incipient turbidity. On cooling, the *ethyl* ester separated in clusters of pale lemon-yellow, woolly needles (1·4 g.), m. p. 198—199° (Found: C, 68·1; H, 5·5; N, 7·2. $C_{23}H_{22}O_5N_2$ requires C, 68·0; H, 5·5; N, 6·9). The corresponding *methyl* ester was obtained by treating either the methyl or the ethyl ester of the azlactone by the method just described, methyl alcohol being used as the solvent; it crystallised from ethyl alcohol in clusters of yellow plates, m. p. 230—231° (decomp.) (Found: C, 66·6; H, 4·6. $C_{21}H_{18}O_5N_2$ requires C, 66·6; H, 4·8%).

2-Carbethoxyindole-3-(α-benzamido)acrylamide.—The ethyl ester of the azlactone (0·5 g.) was refluxed with ethyl alcohol (8 c.c.) containing concentrated aqueous ammonia (3 c.c.). After 40 minutes the solution was cooled, and the crystalline *amide* (0·4 g.) collected; it crystallised from ethyl alcohol, in which it was sparingly soluble, in fine colourless needles, m. p. 246—247°, resolidifying to a scarlet solid at 249° (Found: C, 66·6; H, 5·0; N, 11·1. $C_{21}H_{19}O_4N_3$ requires C, 66·8; H, 5·1; N, 11·1%). The amide dissolves in hot 2*N*-sodium hydroxide to give a deep orange-red solution, which yields an orange-yellow crystalline precipitate on passage of carbon dioxide. This solid was the *trihydrated sodium* salt of *5-keto-2-phenyl-4-(2'-carboxyindolylidene)-4:5-dihydroglyoxaline* (Found: C, 56·3; H, 4·6; N, 10·7; Na, 4·8. $C_{19}H_{12}O_3N_3Na,3H_2O$ requires C, 56·0; H, 4·5; N, 10·3; Na, 5·6%). When an aqueous solution of this salt was acidified with mineral acid, the free *dihydroglyoxalone* separated as an amorphous scarlet precipitate, insoluble in organic solvents (Found: loss at 100°, 2·3; C, 66·3; H, 4·1. $C_{19}H_{13}O_3N_3,\frac{1}{2}H_2O$ requires H_2O, 2·6; C, 67·0; H, 4·1%).

Action of Methyl-alcoholic Potassium Hydroxide on 2-Phenyl-4-(2'-carbethoxyindolylidene)-oxazolone.—The deep red solution formed by dissolving the azlactone (50 g.) in methyl alcohol (1000 c.c.) containing dissolved potassium hydroxide (100 g.) was gently boiled for 3·5 hours,

the crystalline potassium salt of *2-keto-2 : 3-dihydro-β-carboline-4-carboxylic acid* (V) appearing as fine needles on the walls of the flask within 30 minutes. The potassium salt was collected, dried, and ground with dilute hydrochloric acid. The carbolone acid was washed, dried (yield, 7·7 g.), redissolved in boiling 2*N*-potassium hydroxide and precipitated with dilute hydrochloric acid as a gelatinous mass, which passed into a pale brown, amorphous powder on keeping in contact with the solution. It crystallised from boiling ethyl alcohol, in which it was very sparingly soluble, in thin, colourless, rectangular plates, m. p. 365° (decomp.) after darkening at 340° (Found: C, 62·9; H, 3·4; N, 12·3. $C_{12}H_8O_3N_2$ requires C, 63·1; H, 3·5; N, 12·3%), insoluble in all the common organic solvents except ethyl alcohol or glacial acetic acid and giving a brownish-purple colour with alcoholic ferric chloride. The acid has no basic properties; it is not soluble in sodium hydrogen carbonate solution but loses its crystalline form, especially on warming, with formation of a sodium salt. The *methyl* ester was formed by refluxing the acid (1 g.) with methyl alcohol (16 c.c.) containing sulphuric acid (4 c.c.) and gradually separated in colourless needles (1·0 g.), m. p. 272—273°, soluble in 200 parts of boiling methyl alcohol (Found: C, 64·5; H, 4·3; N, 11·7. $C_{13}H_{10}O_3N_2$ requires C, 64·5; H, 4·1; N, 11·6%). On hydrolysis with methyl-alcoholic potassium hydroxide the original acid was recovered, first as the sparingly soluble potassium salt and then as the acid, which was characterised as the ethyl ester. The *ethyl* ester, prepared in the same way, separated from ethyl alcohol in thin colourless diamond-shaped plates, m. p. 260—261° (Found: C, 65·3; H, 4·9. $C_{14}H_{12}O_3N_2$ requires C, 65·6; H, 4·7%).

The methyl-alcoholic filtrate after removal of the potassium salt was concentrated under reduced pressure to one-half its original volume, diluted with 2 volumes of water, and alkalinity to litmus exactly removed by addition of dilute hydrochloric acid, any local acidity being avoided by vigorous stirring. The crystalline precipitate (20·9 g.) of *methyl 2-keto-2 : 3-dihydro-β-carboline-4-orthoformate* (VI, R = Me), after several crystallisations from ethyl alcohol, had m. p. 233—234° (decomp.). It crystallised from alcohol as a mixture of clusters of colourless needles and bold prisms, but if the solution was allowed to cool very slowly, well-formed bold prisms containing one molecule of ethyl alcohol of crystallisation separated. The needle form had m. p. 232—233° and did not depress the m. p. of the prisms; on standing in contact with alcohol, it slowly changed into bold prisms (Found for fresh air-dried material: C, 61·1; H, 6·5; loss at 110°, 13·8; *O*-alkyl, calc. as OMe, 36·0. $C_{15}H_{16}O_4N_2,C_2H_5{\cdot}OH$ requires C, 61·1; H, 6·6; $C_2H_5{\cdot}OH$, 13·8; 3OMe, 1OEt, calc. as 4OMe, 37·1%. Found for material dried at 110°: C, 62·5; H, 5·4; N, 9·7; OMe, 31·8. $C_{15}H_{16}O_4N_2$ requires C, 62·5; H, 5·5; N, 9·7; 3OMe, 32·3%). In both Zeisel determinations the demethylated product was identified as the carboxycarbolone, m. p. 365°, and by conversion into the methyl ester, m. p. 272—273°. The orthoformic ester gives a deep purple colour with alcoholic ferric chloride, and a diffused pink band on long standing with an alcoholic solution of *p*-dimethylaminobenzaldehyde in contact with sulphuric acid. Cold dilute hydrochloric acid has no visible effect on the orthoformate, but on warming for a few minutes there is a rapid quantitative conversion of the solid into needles of the methyl ester of the carboxycarbolone, identical in all respects with that described above. The orthoformate is also unaffected by 2*N*-potassium hydroxide at room temperature, but on boiling gives a quantitative yield of the potassium salt of the carboxycarbolone.

The main aqueous alcoholic filtrate from the preparation of the orthoformate was concentrated under reduced pressure, and a further small quantity of orthoformate removed. The aqueous solution was now acidified to Congo-paper, and the orange-yellow crystalline precipitate (17·0 g.) collected. Ethereal extraction of the mother-liquor gave 6·0 g. of solid material, which was added to the precipitate. On exhaustive extraction (Soxhlet) with low-boiling petroleum, benzoic acid (13·3 g.) was removed and the residue, on solution in acetone, left a small quantity of carboxycarbolone (1·1 g.). The acetone liquor on concentration gave 2-carboxyindole-3-(α-benzamido)acrylic acid (IV) (3·2 g.). The residue (4·6 g.) obtained on complete removal of acetone probably contained 2-carboxyindole-3-pyruvic acid, as it readily gave crystalline derivatives with dinitrophenylhydrazine and thiosemicarbazide. The thiosemicarbazone, pale yellow needles, m. p. 267—268°, was the most characteristic derivative, but was not obtained analytically pure.

Action of Methyl-alcoholic Potassium Hydroxide on 2-Phenyl-4-(2′-carbomethoxyindolylidene)oxazolone.—The azlactone (8 g.) was digested with 10% methyl-alcoholic potassium hydroxide as described above for the ethyl ester. 2-Keto-2 : 3-dihydro-β-carboline-4-carboxylic acid (1·1 g.) was obtained through the potassium salt. It had m. p. 365° (decomp.) and was identical in all respects with that previously described. From the mother-liquors, methyl

2-keto-2 : 3-dihydro-β-carboline-4-orthoformate (3·65 g.) was obtained; on crystallisation from ethyl alcohol it had m. p. 234—235° (decomp.), not depressed by the orthoformate obtained from the ethyl ester.

Action of Sodium Methoxide in Methyl Alcohol on 2-Phenyl-4-(2'-carbethoxyindolylidene)-oxazolone.—The azlactone (5·0 g.) in methyl alcohol (100 c.c.) in which sodium (5 g.) had been dissolved was digested on the water-bath for 3 hours. The solid material (5·4 g.) which had separated was collected, ground with dilute hydrochloric acid, washed with water, and extracted with dilute aqueous ammonia. The solid (2·1 g.) undissolved by the ammonia solution was crystallised from ethyl alcohol and proved to be methyl 2-keto-2 : 3-dihydro-β-carboline-4-orthoformate. The ammoniacal liquor on acidification gave 2-keto-2 : 3-dihydro-β-carboline-4-carboxylic acid (0·9 g.), which was obtained crystalline, m. p. 365° (decomp.), by boiling with ethyl alcohol.

Potassium Derivative of Methyl 2-Keto-2 : 3-dihydro-β-carboline-4-orthoformate.—The orthoformate (1 g.), heated in 2*N*-potassium hydroxide (20 c.c.) to 65—70°, dissolved and, on cooling, the *potassium* derivative crystallised in thin, colourless, hexagonal plates, which were collected and dried on porous tile. The salt was partly hydrolysed by water and the potassium could be estimated by titration with *N*/10-hydrochloric acid (Found: K, 9·0, 8·9; loss at 110°, 21·9. $C_{15}H_{15}O_4N_2K,6H_2O$ requires K, 9·0; $5H_2O$, 20·7%. Found for material dried at 110°: K, 11·6, 11·2; MeO, 27·1. $C_{15}H_{15}O_4N_2K,H_2O$ requires K, 11·4; 3MeO, 27·0%). The potassium salt was decomposed by carbon dioxide, and the methyl orthoformate recovered unchanged. The solid recovered from the Zeisel determination was identified as the carboxycarbolone, m. p. 365° (decomp.), and confirmed by conversion into the methyl ester. The insoluble material from the potassium estimations was collected in each case and identified as unchanged orthoformate. The *sodium* derivative, prepared in a similar way, crystallised in thin hexagonal plates (Found: loss at 110°, 26·5. $C_{15}H_{15}O_4N_2Na,6H_2O$ requires H_2O, 25·8%. Found for dried material: Na, 7·0. $C_{15}H_{15}O_4N_2Na$ requires Na, 7·4%).

Methyl 2-Keto-3-methyl-2 : 3-dihydro-β-carboline-4-orthoformate (IX).—(a) The dried potassium derivative of the methyl orthoformate (1·1 g.) was refluxed with excess of methyl iodide for 3 hours. After removal of solvent, the gummy product was treated with water to remove potassium iodide, and the residual syrup dissolved in ethyl alcohol. The *3-methyl orthoformate* (IX) crystallised in stout, colourless, square plates (0·55 g.) and after five crystallisations from alcohol had m. p. 262—263° (with slight darkening and decomp.) (Found: C, 62·9, 63·5; H, 5·8, 6·2, 6·0; N, 9·6; MeO, 30·4, 29·5; MeN, 5·6, 7·0. $C_{16}H_{18}O_4N_2$ requires C, 63·5; H, 6·0; N, 9·3; 3MeO, 30·8; MeN, 9·6%). This product appeared to contain a trace of unmethylated material, as shown by a deepening of colour with a trace of ferric chloride and by the abnormally low m. p. (see below). By gentle warming with dilute hydrochloric acid the methylation product was transformed practically quantitatively into *methyl 2-keto-3-methyl-2 : 3-dihydro-β-carboline-4-carboxylate* (VIII, R = Me), which formed clusters of colourless needles, m. p. 256—258°, from alcohol (Found: C, 65·3, 65·3; H, 4·9, 4·7; MeO, 11·2, 11·5. $C_{14}H_{12}O_3N_2$ requires C, 65·6; H, 4·7; MeO, 12·1%), and did not give a colour with alcoholic ferric chloride.

(b) The methyl orthoformate (0·2 g.) in methyl alcohol (20 c.c.) was treated with diazomethane (5 mols.) in ether (150 c.c.), and the mixture kept for 24 hours. On removal of most of the solvents, the product (IX) (0·18 g.) crystallised in rectangular plates, m. p. 283—284° (Found: C, 63·8; H, 6·3; MeO, 30·6; MeN, 6·1%). It gave no coloration with alcoholic ferric chloride. A mixture of the two products obtained by (a) and (b) melted at 262—264° (with slight darkening and decomp.). When (b) was treated with warm dilute hydrochloric acid, a quantitative conversion into the methyl ester (VIII) was obtained. The product crystallised from ethyl alcohol in clusters of colourless needles, m. p. 258—259°, not depressed by the ester obtained under (a), and gave no coloration with alcoholic ferric chloride.

Methyl 2-Keto-1 : 3-dimethyl-2 : 3-dihydro-β-carboline-4-carboxylate (X).—The parent methyl orthoformate (1·8 g.) was dissolved in boiling dry acetone (125 c.c.), anhydrous potassium carbonate (20 g.) and methyl sulphate (6 c.c.) added, and the mixture refluxed for 3 hours. The filtrate was concentrated (50 c.c.) and, on cooling, the *ester* (X) crystallised in fine colourless needles (1·2 g.). Recrystallisation from ethyl alcohol gave a felt of long, fine, silky needles, m. p. 160—161° (Found: C, 66·5; H, 5·4; MeO, 11·4; MeN, 12·6. $C_{15}H_{14}O_3N_2$ requires C, 66·6; H, 5·2; MeO, 11·5; 2MeN, 21·5%).

Action of Ethyl-alcoholic Potassium Hydroxide on 2-Phenyl-4-(2'-carbethoxyindolylidene)-oxazolone.—The oxazolone (5 g.) was refluxed with ethyl alcohol (100 c.c.) containing potassium hydroxide (10 g.) for 3·5 hours, and the products isolated by methods similar to those already described. The normal carboxycarbolone, m. p. 365°, was identified as its methyl ester. For

the isolation of *ethyl 2-keto-2 : 3-dihydro-β-carboline-4-orthoformate* (VI, R = Et) great care had to be exercised, as traces of acid in excess tended to hydrolyse it to the carbethoxycarbolone. In practice, dilute hydrochloric acid was added to the aqueous alcoholic solution until it was only faintly alkaline; the ethyl orthoformate (1·8 g.) then separated as a crystalline powder. From ethyl alcohol, in which it was readily soluble, it separated in slender colourless prisms, m. p. 192—193° (Found : loss at 100°, 5·3, 5·4. $C_{18}H_{22}O_4N_2,\frac{1}{2}C_2H_5\cdot OH$ requires loss, 6·5%. Found for the dried solid : C, 65·9, 65·1; H, 6·8, 6·8; N, 8·8; EtO, 37·0, 38·6, 37·0. $C_{18}H_{22}O_4N_2$ requires C, 65·7; H, 6·7; N, 8·4; 3EtO, 40·5%). The product recovered from the Zeisel determination had m. p. 365° (decomp.) and was identified through its methyl ester as the carboxycarbolone. The ethyl orthoformate was very much more readily soluble than the corresponding methyl derivative. In alcoholic solution it gave a purple colour with a trace of ferric chloride. It was more readily decomposed than the methyl derivative by dilute acids, 2*N*-hydrochloric acid hydrolysing it at room temperature. Ethyl 2-keto-2 : 3-dihydro-β-carboline-4-carboxylate, thus produced in quantitative yield, crystallised from ethyl alcohol in diamond-shaped plates, m. p. 261—262°, not depressed by the ethyl ester prepared by direct esterification of the acid.

Methyl 2-Chloro-β-carboline-4-carboxylate (XI).—Finely powdered 2-keto-2 : 3-dihydro-β-carboline-4-carboxylic acid (10 g.) was mixed with phosphorus pentachloride (20 g.; 2·2 mols.), and phosphorus oxychloride (30 c.c.) added. The mixture was heated on a vigorously boiling water-bath for 2·5 hours. The solvent was removed by distillation under reduced pressure and then by addition of dry benzene, which was similarly removed. Methyl alcohol (150 c.c.) was added to the residual, partly solid mass, and the mixture refluxed for an hour, the colour changing from purple to dark greenish-brown. The solution was filtered hot from a small quantity of insoluble substance and allowed to crystallise. The cream-coloured needles which separated were fractionally crystallised from ethyl acetate and gave as the major product *methyl 2-chloro-β-carboline-4-carboxylate* in clusters of thin rectangular plates, m. p. 244—245° (Found : C, 59·6; H, 3·5; OMe, 10·4; Cl, 14·2. $C_{13}H_9O_2N_2Cl$ requires C, 59·9; H, 3·5; OMe, 11·9; Cl, 13·6%). On solution in concentrated hydrochloric acid a hydrochloride was formed, m. p. 231—232° (decomp.), crystallising in yellow rectangular plates, decomposed by alcohol with liberation of unchanged ester.

On hydrolysis of the methyl chloro-ester (0·5 g.) with hot 2*N*-sodium hydroxide (15 c.c.) and acidification a partly crystalline precipitate (0·45 g.) was obtained, which on crystallisation from 50% aqueous ethyl alcohol gave *2-chloro-β-carboline-4-carboxylic acid*, m. p. 246—247° (decomp.), as a felt of long fine colourless needles which only showed a trace of fluorescence in solution (Found : loss at 110°, 7·9. $C_{12}H_7O_2N_2Cl,H_2O$ requires H_2O, 6·8%. Found for the dried solid : C, 58·1; H, 3·0; N, 11·0. $C_{12}H_7O_2N_2Cl$ requires C, 58·4; H, 2·9; N, 11·4%). On re-esterification the original methyl ester was obtained.

When the original methyl-alcoholic mother-liquor from which the crude methyl chloro-ester had crystallised was concentrated, a bright yellow, crystalline *dihydrochloride* (3·6 g.) separated, m. p. 213—214° (decomp.) (Found : C, 58·2; H, 4·1; N, 10·4. $C_{25}H_{20}O_4N_4,2HCl$ requires C, 58·5; H, 4·3; N, 10·9%). When treated with methyl or ethyl alcohol, it became white and amorphous, m. p. 303—304° (decomp.). The amorphous base was almost insoluble in the usual solvents and very sparingly soluble in glacial acetic acid, from which it separated in fine colourless needles, m. p. 317—318° (decomp.). The yellow hydrochloride and the amorphous base were soluble in boiling pyridine and the solution when kept slowly deposited the *base* in colourless, well-formed, rectangular tablets, m. p. 333—334° (decomp.) (Found : C, 68·0, 68·0; H, 4·5, 4·4; N, 13·0; MeO, 10·0. $C_{25}H_{20}O_4N_4$ requires C, 68·1; H, 4·6; N, 12·7; 2MeO, 14·1%).

On addition of water to the methyl-alcoholic mother-liquor after removal of the yellow hydrochloride, a further quantity of methyl 2-chloro-β-carboline-4-carboxylate was obtained, the total yield being thus brought up to 45%.

Reduction of Methyl 2-Chloro-β-carboline-4-carboxylate.—The methyl chloro-ester (1·0 g.) was heated with hydriodic acid (6 c.c.; *d* 1·7), red phosphorus (0·4 g.), and potassium iodide (0·4 g.) in a sealed tube at 180° for 6·5 hours. The crystalline solid was collected, dissolved in dilute sodium hydroxide solution, and precipitated with dilute acetic acid. The product, *norharmancarboxylic acid*, pale yellow needles (0·8 g.), was sparingly soluble in glacial acetic acid, from which it separated in lemon-yellow rhomboidal plates, m. p. 309—310° (decomp.) (Found : loss at 110°, 29·9. $C_{12}H_8O_2N_2,1\cdot5CH_3\cdot CO_2H$ requires $CH_3\cdot CO_2H$, 29·8%. Found for the dried solid : C, 67·4; H, 3·8; N, 13·3. $C_{12}H_8O_2N_2$ requires C, 67·9; H, 3·8; N, 13·2%). In dilute mineral acids norharmancarboxylic acid exhibited a blue fluorescence. The *methyl*

ester (XII, R = H; R′ = Me) was prepared when the acid (0·2 g.) was refluxed with methyl alcohol (8 c.c.) and sulphuric acid (2 c.c.) for 3·5 hours. The cooled solution was diluted with water and made faintly alkaline with ammonia. The finely divided precipitate crystallised from benzene, in which it was sparingly soluble, in small colourless needles, m. p. 262° (decomp.). When crystallised from alcohol for analysis, it separated in clusters of flattened needles (Found : C, 69·2; H, 4·9; N, 12·0. $C_{13}H_{10}N_2O_2$ requires C, 69·0; H, 4·5; N, 12·4%).

Action of Diazomethane on Norharmancarboxylic Acid.—The acid (0·2 g.), suspended in methyl alcohol (20 c.c.), was treated with an ethereal solution of diazomethane in excess. After 24 hours the solvents were removed, leaving a bright yellow, crystalline material. By trituration with alcohol the yellow material was removed, leaving a colourless crystalline solid (0·1 g.), which on recrystallisation from benzene gave *methyl* 1-*methyl*-β-*carboline*-4-*carboxylate* (XII, R = R′ = Me), m. p. 256—257°, in fine colourless needles (Found: C, 70·2; H, 5·1. $C_{14}H_{12}O_2N_2$ requires C, 70·0; H, 5·0%). This ester was sparingly soluble in most organic solvents, but dissolved in dilute acids with a yellow colour and bright blue fluorescence.

Decarboxylation of Norharmancarboxylic Acid.—The acid (0·5 g.) was intimately mixed with calcium hydroxide (5 g.) and heated in a distilling flask with a bare flame. The distillate crystallised from benzene in fine colourless needles of norharman (0·34 g.), m. p. 198—199° (Found : C, 78·4; H, 4·8. Calc. : C, 78·5; H, 4·8%). The picrate crystallised from alcohol in bright yellow, feathery needles, m. p. 260—261° (decomp.) (Found : C, 51·3; H, 3·1. Calc. : C, 51·4; H, 2·8%).

2-*Carbethoxyindole*-3-*aldehyde*-p-*nitrophenylhydrazone* (XIII, R = Et).—Prepared from the components in boiling ethyl alcohol, this *hydrazone* separated in brownish-red needles. From boiling glacial acetic acid, in which it was sparingly soluble, it crystallised in bronze needles, m. p. 274—275° (decomp.) but solidifying almost immediately to a yellow mass of needles, m. p. *ca.* 335° (Found : C, 60·9; H, 4·4. $C_{18}H_{16}O_4N_4$ requires C, 61·3; H, 4·6%).

When the hydrazone (0·8 g.) was heated at 290—300° under reduced pressure for 1 hour, it gradually lost its deep red colour and changed into yellow needles. The product was boiled with glacial acetic acid to remove unchanged material and the undissolved material (0·6 g.) was crystallised from pyridine, in which it was moderately easily soluble. The product, 2-p-*nitrophenylindolo*(2′ : 3′ : 4 : 5)*pyridaz*-3-*one* (XIV), was thus obtained in pale fawn-coloured needles, m. p. above 365° (Found : C, 62·7; H, 3·3. $C_{16}H_{10}O_3N_4$ requires C, 62·7; H, 3·3%).

2-*Carbomethoxyindole*-3-*aldehyde*-p-*nitrophenylhydrazone*, prepared similarly, crystallised from glacial acetic acid in crimson needles, which did not melt but passed on heating into almost colourless needles at 287—292° (Found : C, 60·2; H, 4·2. $C_{17}H_{14}O_4N_4$ requires C, 60·3; H, 4·2%). When heated, this hydrazone gave the same indolopyridazone as was obtained from the ethyl ester.

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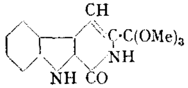
104. *The Hydrolysis of Azlactones with Alcoholic Potassium Hydroxide.*

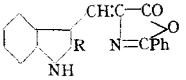
By ERIC T. STILLER.

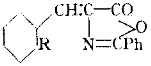
IN view of the isolation of methyl 2-keto-2 : 3-dihydro-β-carboline-4-orthoformate (I) from the hydrolytic products of the azlactone, 2-phenyl-4-(2′-carbomethoxyindolylidene)-oxazolone (II, R = CO_2Me), with alcoholic potassium hydroxide (King and Stiller, preceding paper), it was desirable to examine other azlactones when subjected to similar hydrolytic conditions.

When 2-phenyl-4-(*o*-carbomethoxybenzylidene)oxazolone (III, R = CO_2Me), prepared from methyl phthalaldehydate by condensation with hippuric acid in the presence of acetic anhydride (Bain, Perkin and Robinson, J., 1914, **105**, 2397), was hydrolysed by 10% methyl-alcoholic potassium hydroxide, the principal product was *methyl* 1-*keto*-1 : 2-*dihydroisoquinoline*-3-*orthoformate* (IV; R = Me, R′ = H). The properties of this substance were in all respects analogous to those of the corresponding methyl ketocarbolineorthoformate

(I). It was hydrolysed by dilute acids slowly in the cold and rapidly when warmed to give *methyl* iso*carbostyril-3-carboxylate* (V; R = Me, R′ = H). On warming with dilute aqueous

(I.) 

 (II.)



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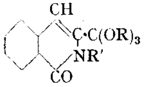
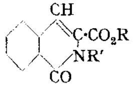


(IV.)



(V.)

potassium hydroxide, it formed a crystalline *potassium* derivative, but prolonged heating converted it into *iso*carbostyril-3-carboxylic acid. By the action of diazomethane *methyl* 1-*keto*-2-*methyl*-1 : 2-*dihydro*iso*quinoline*-3-*orthoformate* (IV; R = R′ = Me) was produced, which on hydrolysis with dilute acid readily gave *methyl* 1-*keto*-2-*methyl*-1 : 2-*dihydro*iso*quinoline*-3-*carboxylate* (V; R = R′ = Me).

The corresponding *ethyl* 1-*keto*-1 : 2-*dihydro*iso*quinoline*-3-*orthoformate* (IV; R = Et, R′ = H) was formed when ethyl alcohol was substituted for methyl alcohol in the hydrolysis of 2-phenyl-4-(*o*-carbomethoxybenzylidene)oxazolone (III, R = CO_2Me). Its properties were completely analogous to those described above for the methyl orthoformate.

The mechanism of the formation of these orthoformates appears to require a carbalkoxy-group R (II or III) on the adjacent nuclear carbon atom, since 2-phenyl-4-benzylideneoxazolone (III, R = H) and 2-phenyl-4-indolylideneoxazolone (II, R = H) gave normal products, namely, α-benzamidocinnamic acid and indole-3-(α-benzamido)acrylic acid respectively.

Beattie (*Amer. Chem. J.*, 1908, **40**, 424) has reported the isolation of an inseparable mixture of methyl and ethyl *iso*carbostyril-3-carboxylates as abnormal constituents of a fasciated variety of *Anemone thalictroides* L. (Rue anemone). *iso*Carbostyrilcarboxylic acid was not esterified when treated with alcohol containing normal concentrations of sulphuric acid (5—10%), but when methyl or ethyl alcohol containing 35—40% of sulphuric acid was used, esterification proceeded smoothly and gave quantitative yields of the methyl or the *ethyl* ester of *iso*carbostyrilcarboxylic acid.

Experimental.

Action of Methyl-alcoholic Potassium Hydroxide on 2-Phenyl-4-(o-carbomethoxybenzylidene)-oxazolone.—The oxazolone (7·4 g.) (Bain, Perkin, and Robinson, *loc. cit.*) was dissolved in methyl alcohol (140 c.c.) containing potassium hydroxide (7 g.), and the yellowish-green solution refluxed for 3 hours. A third of the methyl alcohol was removed by distillation, and water (3 vols.) added to the clear cooled solution, which was then neutralised to litmus by the addition of dilute hydrochloric acid, local acidity being prevented by vigorous stirring. The crystalline *methyl* 1-*keto*-1 : 2-*dihydro*iso*quinoline*-3-*orthoformate* (IV; R = Me, R′ = H) was collected after standing overnight (yield 4·1 g.), and a further quantity (0·6 g.) obtained by extracting the filtrate with ether. The two crops were combined and dissolved in methyl alcohol and warm water was added until crystallisation commenced; thin hexagonal plates, m. p. 134—135°, were then obtained (Found : C, 62·8; H, 6·2; OMe, 36·5. $C_{13}H_{15}O_4N$ requires C, 62·6; H, 6·1; OMe, 37·4%), readily soluble in ethyl and methyl alcohol, acetone, and benzene, less readily in ether and light petroleum, and insoluble in water, sodium bicarbonate and cold 2*N*-potassium hydroxide solutions. In alcoholic solution the yellow colour of ferric chloride is intensified. When the orthoformate is boiled with 2*N*-potassium hydroxide for a prolonged period (2 hours), *iso*carbostyril-3-carboxylic acid is produced, m. p. and mixed m. p. 325—326° (decomp.) (Bamberger and Kitschelt, *Ber.*, 1892, **25**, 1143, give m. p. 320°). Cold dilute hydrochloric acid gradually converts the orthoformate into methyl *iso*carbostyril-3-carboxylate, m. p. and mixed m. p. 161—162°. The hydrolysis is complete and quantitative when a suspension of the orthoformate in dilute hydrochloric acid is warmed on the water-bath for a few minutes.

The alcohol from the original neutral aqueous alcoholic filtrate after the separation of the methyl orthoformate was removed by distillation under reduced pressure, and the solution acidified with dilute hydrochloric acid. The colourless crystalline precipitate was collected, dried, and extracted with boiling petrol, which removed benzoic acid. The residual *iso*carbostyril-3-carboxylic acid (0·26 g.) was recrystallised from acetone and had m. p. 325—326° (decomp.) (Found : C, 63·6; H, 4·1. Calc. : 63·4; H, 3·7%). The *methyl* ester was prepared by refluxing *iso*carbostyril-3-carboxylic acid (0·2 g.) with methyl alcohol (8 c.c.) and concentrated sulphuric acid (2 c.c.) for 2 hours; the cooled solution was diluted with water and the needles obtained were recrystallised from alcohol, giving long, fine, colourless needles, m. p. 161—162° (Found : C, 65·1; H, 4·5; OMe, 15·0. $C_{11}H_9O_3N$ requires C, 65·0; H, 4·5; OMe, 15·3%). The *ethyl* ester, obtained in quantitative yield in a similar manner, crystallised from alcohol in aggregates of colourless tablets, m. p. 147—148° (Found : C, 66·3; H, 5·0. $C_{12}H_{11}O_3N$ requires C, 66·3; H, 5·1%). The *amide* was prepared by treating the methyl ester (1·8 g.) with concentrated aqueous ammonia (30 c.c., *d* 0·880) for 2 hours in a sealed bottle at room temperature, the long needles changing to small rectangular plates; these (1·5 g.) were recrystallised twice from glacial acetic acid and then had m. p. 289° (decomp.) (Found : C, 63·6; H, 4·3. $C_{10}H_8O_2N_2$ requires C, 63·8; H, 4·3%).

Potassium Derivative of Methyl 1-*Keto*-1 : 2-*dihydro*iso*quinoline*-3-*orthoformate* (IV; R = Me, R′ = K). The orthoformate (0·5 g.) was dissolved in 2*N*-potassium hydroxide (5 c.c.) at 65—70°; on cooling, the *potassium* derivative (0·65 g.) crystallised in colourless prismatic needles, which were dried on porous tile. The derivative is decomposed by water, giving the methyl orthoformate, and the potassium can be estimated by titration with *N*/10-hydrochloric acid (Found: loss at 110°, 17·7. $C_{13}H_{14}O_4NK,3\frac{1}{2}H_2O$ requires H_2O, 18·0%. Found for material dried at 110° : K, 13·5, 13·7 ; OMe, 31·2. $C_{13}H_{14}O_4NK$ requires K, 13·6; OMe, 32·4%).

Methyl 1-*Keto*-2-*methyl*-1 : 2-*dihydro*iso*quinoline*-3-*orthoformate* (IV; R = R′ = Me).—(a) The methyl orthoformate (0·6 g.), dissolved in methyl alcohol (30 c.c.), was treated with diazomethane (5 mols.) in dry ether (100 c.c.) and after 24 hours the solvents were distilled. The residue was very soluble in all organic solvents and crystallised from 50% aqueous methyl alcohol in colourless, laminated, rectangular plates of *methyl* 1-*keto*-2-*methyl*-1 : 2-*dihydro*iso*quinoline*-3-*orthoformate*, m. p. 87—88° (Found : C, 63·7; H, 6·4; OMe, 35·4; NMe, 8·2. $C_{14}H_{17}O_4N$ requires C, 63·8; H, 6·5; OMe, 35·4; NMe, 11·0%), which gave no coloration with alcoholic ferric chloride. This *N*-methyl derivative, gently warmed in dilute hydrochloric acid, was quantitatively converted into *methyl* 1-*keto*-2-*methyl*-1 : 2-*dihydro*iso*quinoline*-3-*carboxylate* (V; R = R′ = Me), which crystallised from alcohol in aggregates of colourless slender prisms, m. p. 132—133° (Found : C, 66·8; H, 5·2; OMe, 14·1; NMe, 9·3. $C_{12}H_{11}O_3N$ requires C, 66·3; H, 5·1; OMe, 14·3; NMe, 13·4%), and gave no colour with alcoholic ferric chloride.

(b) The dried potassium derivative of methyl 1-keto-1 : 2-dihydro*iso*quinoline-3-orthoformate (1·65 g.) was refluxed with methyl iodide (20 c.c.) for 4 hours, the methyl iodide distilled, and water added to the syrupy product. The aqueous suspension was extracted three times with ether. From the dried extract a viscous syrup was obtained which became partly crystalline after several days. It was treated with dilute hydrochloric acid for a few minutes on the water-bath, and the crystalline solid collected. Fractional crystallisation from alcohol gave methyl *iso*carbostyril-3-carboxylate, m. p. 161—162°, and methyl 2-methyl*iso*carbostyril-3-carboxylate, m. p. and mixed m. p. 132—133°. Hence the syrupy methylation product was a mixture of methyl *iso*carbostyril-3-orthoformate and methyl 2-methyl*iso*carbostyril-3-orthoformate.

Action of Ethyl-alcoholic Potassium Hydroxide on 2-*Phenyl*-4-(o-*carbomethoxybenzylidene*)-*oxazolone*.—The oxazolone (5 g.) was refluxed in ethyl alcohol (100 c.c.) containing potassium hydroxide (5 g.) for 3 hours. The potassium benzoate (1·9 g.) that crystallised during the refluxing and also after cooling was removed, and the alcoholic filtrate diluted with water (3 vols.), cooled, and neutralised to litmus with dilute hydrochloric acid with vigorous stirring. The precipitate of *ethyl* 1-*keto*-1 : 2-*dihydro*iso*quinoline*-3-*orthoformate* (IV; R = Et, R′ = H) (2·6 g.), recrystallised from ethyl alcohol, formed colourless elongated prisms, m. p. 183—185° (Found : C, 66·0; H, 7·1; OEt, 44·1. $C_{16}H_{21}O_4N$ requires C, 65·9; H, 7·2; OEt 46·4%), readily soluble in organic solvents and insoluble in water. When warmed with dilute hydrochloric acid for a few minutes, it was quantitatively converted into ethyl *iso*carbostyril-3-carboxylate, m. p. and mixed m. p. 147—148°. The aqueous alcoholic filtrate after removal of the ethyl orthoformate was freed from alcohol by distillation and acidified with dilute hydrochloric acid, giving *iso*carbostyrilcarboxylic acid (1·7 g.).

Action of Methyl-alcoholic Potassium Hydroxide on 2-*Phenyl*-4-*benzylideneoxazolone* (III; R = H).—The oxazolone (Bain, Perkin, and Robinson, *loc. cit.*) (5 g.) was treated exactly as its

o-carbomethoxy-derivative (p. 474) (methyl alcohol, 100 c.c.; potassium hydroxide, 10 g.). The neutral (litmus) aqueous solution yielded nothing to ether, but when acidified (Congo-red) with dilute hydrochloric acid gave α-benzamidocinnamic acid in fine colourless needles (3·7 g.), m. p. 233—234° (decomp.). This acid (0·5 g.) was heated on the water-bath with acetic anhydride (1 c.c.) for 30 minutes, the cooled solution diluted with water, and the yellow precipitate crystallised from glacial acetic acid; 2-phenyl-4-benzylideneoxazolone was obtained.

Action of Methyl-alcoholic Potassium Hydroxide on 2-Phenyl-4-indolylideneoxazolone.—The azlactone (II; R = H) (1 g.) (Ellinger and Flamand, *Ber.*, 1907, **40**, 3031) was treated with methyl alcohol (20 c.c.) containing potassium hydroxide (2 g.) as in the preceding case. The only product isolated was indole-3-(α-benzamido)acrylic acid (0·87 g.), m. p. 236—237° (decomp.).

I am indebted to Mr. A. W. Hemmings for assistance in the preparation of intermediates.

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London, N.W. 3. [*Received, January 6th*, 1937.]

105. *Studies in Chelation. Part V. Hydroxyacetylhydrindenes.*

By Wilson Baker.

From theoretical considerations Mills and Nixon (J., 1930, 2510) considered it probable that in the molecule of hydrindene the bond common to the two rings is single (as in I and II). This was supported by the facts that both 5-hydroxy- and 5-amino-hydrindene showed chemical reactivity only in position 6 and not in the alternative ortho-position 4. It was, however, pointed out that *o*-4-xylenol also is reactive chiefly in position 6, so that the influences of the hydrindene ring other than a possible strain effect could afford an explanation of the chemical reactivity of the 5-substituted hydrindenes in position 6.

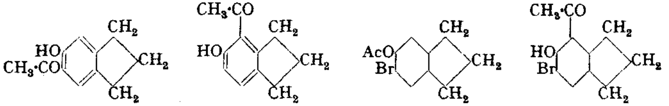
Support for the original hypothesis has been obtained from two independent sources. Sidgwick and Springall (*Chem. and Ind.*, 1936, **55**, 476; J., 1936, 1532) showed that the dipole moment of 5 : 6-dibromohydrindene was in very close agreement with the moment calculated on the assumption of a fixed double bond between carbon atoms 5 and 6, evidence which indicates a fixation of the links in hydrindene in the resting state of the molecule, unlike the previous evidence based on chemical reactivity. The same conclusion was reached by Fieser and Lothrop (*J. Amer. Chem. Soc.*, 1936, **58**, 2050), who observed that 5-hydroxy-6-methylhydrindene refuses to couple with diazo-compounds, though 5-hydroxy-4 : 7-dimethylhydrindene couples readily in position 6.

To obtain further evidence on the structure of hydrindene, 5-*hydroxy*-6-*acetylhydrindene* (I) and 5-*hydroxy*-4-*acetylhydrindene* (II) were examined. It has been shown (Parts I, II, and III, Baker, J., 1934, 1684; Baker and Lothian, J., 1935, 628; 1936, 274) that chelation between the hydroxyl and the acetyl group in *o*-hydroxyacetophenones and in β-hydroxy-ketones depends upon the presence of a double bond between the carbon atoms bearing these groups,* and this fact furnishes a new method for the detection of a fixed double or single link in a simple aromatic structure. Moreover this method is free from certain objections (Sutton and Pauling, *Trans. Faraday Soc.*, 1935, **31**, 939) which can be raised against arguments based on the formation in preponderating amount of one product in a chemical reaction in cases where two isomers might be produced (Mills and Nixon, *loc. cit.*). Such objections can hardly apply, however, to the experiments of Fieser and Lothrop (*loc. cit.*).

If fixation of the aromatic links in compounds (I) and (II) occurs as postulated by Mills and Nixon, then it is evident that 5-hydroxy-6-acetylhydrindene (I) should exhibit a greater degree of chelation than 5-hydroxy-4-acetylhydrindene (II). It must be pointed out, however, that even if in simple hydrindenes the double bonds are definitely fixed as in (I) and (II), in the case of the hydroxyacetylhydrindene (II) it is not to be expected that the compound will behave like a completely non-chelated compound, since chelation between

* The reason for this which was advanced in Part I requires a slightly new interpretation in view of our increased knowledge of the nature of "co-ordinately linked hydrogen" (see Sidgwick, *Ann. Reports*, 1934, **31**, 41).

hydroxyl and acetyl groups may well be a more powerful influence in fixing the bonds in an aromatic nucleus than fusion with a *cyclo*pentane ring. In the case of (I) these two effects reinforce each other, in the case of (II) they are in opposition.



(I.) (II.) (III.) (IV.)

Examination of the physical properties of (I) and (II) shows that both are considerably chelated, but that (II) is less highly chelated than (I) in accordance with expectation. (I) is readily soluble in light petroleum and benzene, and easily volatile in steam, (II) is very much less soluble in hydrocarbon solvents (probably partly explicable by its higher m. p., which may itself be due to its greater association) and almost involatile in steam. The following table gives some of the physical properties of the two compounds, the difference in degree of chelation being clearly indicated by the greater depression of the melting point of (II) under water as compared with that of (I), in spite of its higher melting point. For purposes of comparison the properties of 5-hydroxyhydrindene are also recorded.

	M. p., dry.	M. p., wet.	Depression.	Critical solution temp.
5-Hydroxy-6-acetylhydrindene (I)	59·5°	57·6°	1·9°	>265°
5-Hydroxy-4-acetylhydrindene (II)	124·5	119	5·5	>265
5-Hydroxyhydrindene	53·5	36·5	17	*ca.* 200

The critical solution temperatures of the compounds (I) and (II) in water could not be reached owing to darkening above 250°. Both give chelate copper derivatives soluble in chloroform.

5-Hydroxy-6-acetylhydrindene (I) was prepared from *5-acetoxyhydrindene* by treatment with aluminium chloride in carbon disulphide, and appeared to be the sole product of the reaction. The position of the acetyl group is inferred from the known reactivity of 5-hydroxyhydrindene in position 6 and by the fact that the compound differs from 5-hydroxy-4-acetylhydrindene (II), which was prepared by the following method.

5-Hydroxyhydrindene was converted into 6-bromo-5-hydroxyhydrindene (Mills and Nixon, *loc. cit.*; these authors established the position of the bromine atom in this compound), and thence by acetylation into *6-bromo-5-acetoxyhydrindene* (III). Compound (III) when heated with aluminium chloride in carbon disulphide underwent slow conversion into *6-bromo-5-hydroxy-4-acetylhydrindene* (IV), which when reduced with zinc dust in sodium hydroxide solution gave 5-hydroxy-4-acetylhydrindene (II). Confirmation of the position of the acetyl group in this compound was afforded by the fact that, whilst (IV), in which the carbonyl group might be expected to be sterically hindered by the methylene group in position 3, merely suffers loss of the bromine atom when reduced with zinc dust and sodium hydroxide, 5-hydroxy-6-acetylhydrindene (I), where such a steric effect could not be operative, is reduced under exactly the same conditions to the corresponding pinacol. This observation will be the subject of a further communication. The formation of (IV) from (III) is a noticeably much slower reaction than the conversion of 5-acetoxyhydrindene into (I), a result to be expected if the double bonds are fixed, and which may be compared with the experiments of Fieser and Lothrop to which reference has already been made.

An isomer of (IV) of unknown constitution, whose chemical properties are identical with those of (IV), was produced in one reaction when (III) was heated with aluminium chloride and carbon disulphide for a much longer period than normal.

Experimental.

5-Aminohydrindene.—Hydrindene (313 g.) gave 5-acetylhydrindene (313 g.) and thence the oxime (295 g.) [acetylhydrindene (100 g.), alcohol (500 c.c.), water (300 c.c.), hydroxylamine hydrochloride (75 g.), and crystalline sodium acetate (200 g.), heated on the steam-bath for 4 hours, cooled, product collected]. The oxime gave 5-acetamidohydrindene (252 g.) [oxime

(80 g.) was added to a mixture of acetic acid (720 g.) and acetic anhydride (280 g.), saturated with dry hydrogen chloride at 0°, and after 48 hours the crystals of a hydrochloride were isolated, stirred into water, collected and washed], and then 5-aminohydrindene (176 g.) by hydrolysis for 2 hours with four times its weight of concentrated hydrochloric acid on the water-bath, addition of alkali, extraction with ether, and distillation (cf. Borsche and Pommer, *Ber.*, 1921, **54**, 107).

5-Hydroxyhydrindene.—This compound was prepared from 5-aminohydrindene, as a quantity of this substance was available. It is, however, most readily obtained from hydrindene *via* the 5-sulphonic acid (Cook and Linstead, J., 1934, 952). Borsche and John (*Ber.*, 1924, **57**, 658) obtained only a 17% yield from 5-aminohydrindene. 5-Aminohydrindene (16 g.) was dissolved in water (140 c.c.) and concentrated sulphuric acid (25 c.c.), rapidly cooled to − 10°, and a solution of sodium nitrite (8·4 g.) in water (40 c.c.) slowly added. The diazo-solution was run into aqueous copper sulphate (200 c.c. saturated at 15°) through which steam was passing, and 5-hydroxyhydrindene, m. p. 53·5°, was extracted from the distillate with ether (yield 11 g.; 69%).

5-Acetoxyhydrindene.—To a solution of 5-hydroxyhydrindene (10 g.) in *N*-sodium hydroxide (90 c.c.; 1·2 mols.) was added ice, and then acetic anhydride (8·4 g.; 1·1 mols.) in one portion with vigorous shaking. The oily product was shaken in ether with dilute sodium hydroxide solution, then water, dried by calcium chloride, and distilled. *5-Acetoxyhydrindene* distilled at 136°/18 mm. as a colourless oil with an odour of phenyl acetate (Found: C, 75·2; H, 6·6. $C_{11}H_{12}O_2$ requires C, 75·0; H, 6·8%). It solidified in a freezing mixture and then had m. p. 16—17°. The yield was almost quantitative.

5-Hydroxy-6-acetylhydrindene (I).—5-Acetoxyhydrindene (5 g.), dissolved in carbon disulphide (10 c.c.), was treated with coarsely crushed aluminium chloride (10 g.). After the somewhat vigorous reaction had abated, the mixture was heated on the water-bath for 2 hours and subsequently treated with dilute hydrochloric acid. The oily product was obtained solid (4·4 g.) by steam distillation and after crystallising twice from a small volume of methyl alcohol formed prismatic needles, m. p. 59° (Found: C, 74·9; H, 6·9; *M*, 179. $C_{11}H_{12}O_2$ requires C, 75·0; H, 6·8%; *M*, 176). *5-Hydroxy-6-acetylhydrindene* in alcoholic solution gives with ferric chloride a rather intense reddish-blue colour, becoming slate-grey on dilution with water; with dilute sodium hydroxide solution it gives a very sparingly soluble, yellow sodium salt, and its alcoholic solution when treated with aqueous copper acetate yields a copper derivative dissolving in chloroform with a green colour. For complete purification the substance was converted into its *acetyl* derivative by boiling with excess of acetic anhydride for 4 hours; this separated as a solid when the mixture was shaken with water and crystallised from light petroleum (b. p. 60—80°) in thick diamond-shaped plates, m. p. 88° (Found: C, 71·4; H, 6·9; *M*, 210. $C_{13}H_{14}O_3$ requires C, 71·5; H, 6·4%; *M*, 218). Hydrolysis with dilute alcoholic sodium hydroxide for a few minutes regenerated 5-hydroxy-6-acetylhydrindene (I), which, crystallised from methyl alcohol and then light petroleum (b. p. 40—60°), had m. p. 59·5°.

6-Bromo-5-acetoxyhydrindene (III).—5-Hydroxyhydrindene (10 g.) was converted into 6-bromo-5-hydroxyhydrindene (Mills and Nixon, *loc. cit.*), and thence by refluxing with acetic anhydride (50 c.c.) for 4 hours into *6-bromo-5-acetoxyhydrindene*. After the excess of acetic anhydride, the acetate distilled at 169°/16 mm. as a colourless oil (16·3 g.) (Found: C, 51·6; H, 4·2; Br, 31·6. $C_{11}H_{11}O_2Br$ requires C, 51·8; H, 4·3; Br, 31·4%).

6-Bromo-5-hydroxy-4-acetylhydrindene (IV).—A mixture of 6-bromo-5-acetoxyhydrindene (5 g.), carbon disulphide (10 c.c.), and aluminium chloride was heated on the water-bath for 5 hours and the product was decomposed with very dilute hydrochloric acid, extracted in ether, and shaken with dilute aqueous sodium hydroxide (unchanged 6-bromo-5-acetoxyhydrindene remained in the ethereal layer). Acidification of the yellow aqueous layer gave an oily product, which solidified; crystallised from a little methyl alcohol (yield, 1 g.), and then from light petroleum (b. p. 40—60°), it formed thin yellow prisms, m. p. 102—103° (Found: C, 51·6; H, 4·4; Br, 31·9; *M*, 258. $C_{11}H_{11}O_2Br$ requires C, 51·8; H, 4·3; Br, 31·4%; *M*, 255). When the *compound* was heated with dilute alcoholic potassium hydroxide for 4 hours at 100°, the bromine atom was not eliminated.

Bromohydroxyacetylhydrindene, m. p. 115°.—In an experiment similar to the above, the mixture was heated for 36 hours. The oil resulting from decomposition of the aluminium complex did not solidify and was collected in ether and distilled under diminished pressure, b. p. about 200°/16 mm. The yellow distillate solidified in contact with methyl alcohol, and was crystallised first from methyl alcohol and then light petroleum (b. p. 40—60°) and obtained in colourless prisms, m. p. 115° (Found: C, 51·7; H, 4·2; Br, 31·4; *M*, 255. $C_{11}H_{11}O_2Br$

requires C, 51·8; H, 4·4; Br, 31·4; *M*, 255), depressed to 70—85° by 6-bromo-5-hydroxy-4-acetylhydrindene. The bromine atom in this *substance* was not eliminated by heating with dilute alcoholic potassium hydroxide for 4 hours at 100°. It dissolved in hot dilute sodium hydroxide to a yellow solution, depositing a sparingly soluble, pale yellow sodium salt on cooling. Its alcoholic solution gave a dull purplish colour with ferric chloride.

5-Hydroxy-4-acetylhydrindene (II).—6-Bromo-5-hydroxy-4-acetylhydrindene (IV) (0·35 g.), dissolved in 2% aqueous sodium hydroxide (10 c.c.), was heated for 6 hours on the water-bath with zinc dust (3·5 g.). The filtered solution was acidified, and the resulting solid crystallised twice from dilute alcohol, forming faintly amber-coloured, flat prisms, m. p. 124·5° (Found: C, 75·0; H, 7·0; *M*, 181, 183. $C_{11}H_{12}O_2$ requires C, 75·0; H, 6·8%; *M*, 176). It gave a dull greenish colour with alcoholic ferric chloride, dissolved in sodium hydroxide solution with a pale yellow colour, and in concentrated sulphuric acid a bright lemon-yellow solution was produced which on dilution with a little water became more orange-yellow and then pale violet. Its alcoholic solution when treated with aqueous copper acetate gave a copper derivative, which dissolved in chloroform with a green coloration. 5-Hydroxy-4-acetylhydrindene also was obtained by similar reduction of the bromohydroxyacetylhydrindene, m. p. 115°.

The author's thanks are due to Mr. R. R. Cawthorne, B.A., B.Sc., for preliminary work in the synthesis of 5-hydroxy-6-acetylhydrindene.

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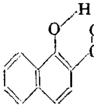
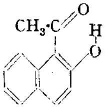
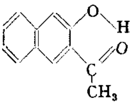
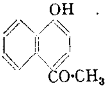
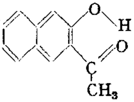
106. *Studies in Chelation. Part VI. Hydroxy-derivatives of Acetylnaphthalenes, Benzonitrile, and Carboxylic Esters.*

By WILSON BAKER and G. N. CARRUTHERS.

Hydroxyacetylnaphthalenes.—The method described in the preceding paper for detecting fixed double and single links in the aromatic nucleus of hydrindene has now been applied to the case of naphthalene. Much evidence has accumulated to show that naphthalene almost invariably reacts as if the bond between carbon atoms 1 and 2 was double, and that between carbon atoms 2 and 3 was single (for a summary of such evidence see Fieser and Lothrop, *J. Amer. Chem. Soc.*, 1935, **57**, 1459), and that this applies to both rings simultaneously is shown by the remarkable behaviour of 2 : 7-dihydroxy-1 : 8-dialkylnaphthalenes, and 2 : 6-dihydroxy-1 : 5-dialkylnaphthalenes which do not couple with diazotised amines and whose allyl ethers do not undergo thermal rearrangement (Fieser and Lothrop, *loc. cit.*). This evidence definitely points to the symmetrical formula for naphthalene (as shown in formulæ I—IV) possessing a double bond common to the two rings. Nevertheless, an *op*-directing group in position 2 in the naphthalene nucleus does occasionally direct an entering substituent into position 3, thus indicating the possibility of a double bond between carbon atoms 2 and 3; examples are (1) the action of carbon dioxide on sodium β-naphthoxide at 280—290°, giving 2-hydroxy-3-naphthoic acid (Schmitt and Burkard, *Ber.*, 1887, **20**, 2702), (2) the bromination o 1-bromo-*p*-toluenesulphon-2-naphthalide in position 3 in pyridine solution (Bell, J., 1932, 2732), and (3) the production in poor yield of a bromobenzohydrindone by ring closure of 1-bromo-2-β-naphthylpropionyl chloride (Mayer and Sieglitz, *Ber.*, 1922, **55**, 1859). The physical evidence as to the structure of naphthalene is conflicting; for a brief discussion of previous work see Hampson and Weissberger (J., 1936, 331). These authors themselves conclude, as a result of the measurement of the dipole moments of chlorinated naphthalenes, that the C–Cl bonds are directed as from the centre of the rings, and that "if there is any fixation of the single and double bonds in naphthalene it is not revealed in the direction of the substituents." On the other hand, Bergmann and Hirshberg (J., 1936, 331), from a study of the dissociation constants of the chloronaphthoic acids, infer that the bond C_1 to C_2 is not identical with the bond C_2 to C_3, and Fries, Bestian, and Klauditz (*Ber.*, 1936, **69**, 715) conclude, from a comparison of the optical properties of *o*-divinylbenzene and naphthalene, that the symmetrical structure is most probably correct.

In order to see if any difference between the links C_1 to C_2 and C_2 to C_3 could be detected

by chelation between hydroxyl and acetyl groups (which has been shown to depend on a double bond between the carbon atoms bearing these groups; for references, see preceding paper), the properties of the four isomeric hydroxyacetylnaphthalenes (I—IV) were investigated. If the symmetrical structure shown in (I—IV), which seems to be

(I.) (II.) (III.) (IV.) (V.)

the most probable and is usually regarded as being due to the tendency for both rings to become as completely aromatic as possible, is quite rigid, it is clear that 2-acetyl-1-naphthol (I) and 1-acetyl-2-naphthol (II) should behave like typically chelated compounds, but that 3-acetyl-2-naphthol (III) should be non-chelated. To provide a reference compound which could not be chelated, the properties of 4-acetyl-1-naphthol (IV) also were examined. The following table gives some of the physical properties of these compounds:

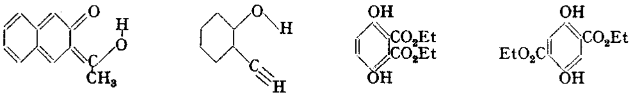
	M. p., dry.	M. p., wet.	Depression.	Critical solution temp.
2-Acetyl-1-naphthol (I)	101°	99°	2°	>255°
1-Acetyl-2-naphthol (II)	64	62	2	*ca.* 234
3-Acetyl-2-naphthol (III)	112	106	6	>255
4-Acetyl-1-naphthol (IV)	197	153	44	*ca.* 212

The only conclusion which can be drawn from these figures is that all three *o*-hydroxyacetylnaphthalenes (I), (II), and (III) are highly chelated compounds. 3-Acetyl-2-naphthol (III) shows a slightly greater depression of the melting point under water than (I) and (II), but on the other hand its critical solution temperature is higher than that of (II). Owing to darkening and decomposition above 250°, the critical solution temperatures of (I) and (III) could not be reached. The great difference between (I), (II), and (III) and the non-chelated compound (IV) is very striking.

The interpretation of the result in the case of 3-acetyl-2-naphthol (III) may mean that chelation between the hydroxyl and the acetyl group is sufficiently powerful to overcome the normal symmetrical arrangement of the naphthalene valencies, so that the molecule must assume the asymmetrical distribution of the bonds as shown in (V) in which one of the rings is *o*-quinonoid. In this connection, it is perhaps significant that 3-acetyl-2-naphthol (III and V) alone amongst the isomeric acetylnaphthols is a highly coloured compound, being bright yellow, and the fact that its methyl ether, in which chelation is impossible, is colourless points to the conclusion that the colour is due to some disturbance of the normal naphthalene structure set up by the process of chelation. On the other hand, it shows none of the properties of a true *o*-quinonoid compound—with bromine it yields a *monobromo*-derivative and not a tetrabromide, and it does not combine additively with maleic anhydride. Again, it would be difficult to account for the fact that 2 : 3-dihydroxynaphthalene does not yield a quinone on oxidation (see Marckwald, *Annalen*, 1893, **274**, 331; 1894, **279**, 1; Fries and Schimmelschmidt, *Ber.*, 1932, **65**, 1502; Fieser, *J. Amer. Chem. Soc.*, 1930, **52**, 5219) if 3-acetyl-2-naphthol actually possessed a fixed *o*-quinonoid structure. The explanation of these facts will probably ultimately be found in the phenomenon of resonance (Pauling and Wheland, *J. Chem. Physics*, 1933, **1**, 362; Sherman, *ibid.*, 1934, **2**, 488); the naphthalene molecule is conceived as a hybrid in which the symmetrical structure (as in I—IV) is the most important, followed in importance by the two asymmetrical structures (as in V). *o*-Quinonoid structures such as (V) and (VI) may be possible as important components of a resonance hybrid (a third component of which is III) which are not possible as the fixed structure of a molecule that does not exhibit resonance (*e.g.*, the unknown naphtha-2 : 3-quinone).

Hydroxybenzonitriles.—Examination of the physical properties of the three isomeric hydroxybenzonitriles has been made in order to find out if the *o*-compound (VII) is capable

of chelation. The substance might contain a hydrogen bond between the oxygen atom and the nitrogen atom which carries the necessary lone pair of electrons; if this were so, then (VII) should possess abnormal physical properties compared with the *m*- and the *p*-



(VI.) (VII.) (VIII.) (IX.)

isomer in which chelation is impossible (as is the case with nitrophenols, hydroxybenzaldehydes, etc.). Experiment showed clearly that the *o*-compound (VII) is in no way abnormal compared with the *m*- and the *p*-compound, as is shown in the following table:

	M. p., dry.	M. p., wet.	Depression.
o-Hydroxybenzonitrile	94·5°	42°	52·5°
m- ,, ...	82	31	51
p- ,, ...	113	61	52

It must, therefore be concluded that *o*-hydroxybenzonitrile is completely non-chelated, a conclusion which has also been reached by Hendricks, Wulf, Hilbert, and Liddel (*J. Amer. Chem. Soc.*, 1936, **58**, 1991), who found that it shows absorption in the infra-red characteristic of the hydroxyl group. They regard the non-chelation of this compound as due to the linear nature of the -C≡N group, owing to which the distance between the nitrogen and oxygen atoms must be rather more than 3 A., a distance greater than the normal length (about 2·6 A.) of a hydrogen bond between oxygen atoms, or between oxygen and nitrogen, a view with which the present authors are in agreement.

Hydroxy-carboxylic Esters.—Evidence as to whether chelation between the carboxylic ester grouping and hydroxyl depends upon the presence of a double bond between the two intermediate carbon atoms is conflicting. (1) In the aliphatic series there is strong evidence that the carbon–carbon double bond is essential. A direct comparison of the b. p.'s of acetoacetic ester (79°/18 mm.*) and β-hydroxybutyric ester (81°/18 mm.) does not appear to support this, but it must be remembered that, even at ordinary pressure, a considerable drop in the b. p. occurs in passing from an unsaturated ester $CHR{:}CH{\cdot}CO_2Et$ to the saturated ester $CH_2R{\cdot}CH_2{\cdot}CO_2Et$; where R is a simple alkyl group, the difference is on the average about 17°. Hence, if β-hydroxybutyric ester were chelated, it should have a b. p. of the order of 20° *lower* than that of acetoacetic ester, whereas in fact its b. p. is slightly higher. The general properties of β-hydroxybutyric ester leave no doubt that it is non-chelated: it is a somewhat viscous liquid, totally miscible with water, and gives no chelate metallic derivatives, properties which stand in strong contrast to those of acetoacetic ester. (2) In the aromatic series the fact that β-resorcylic acid and ester substitute in position 5 and not in position 2 would appear to indicate that fixation of the Kekulé forms as a result of such chelation does not take place as in the case of *o*-hydroxycarbonyl compounds (Baker, J., 1934, 1689), but such evidence is valueless if the reagent which is used to bring about the substitution is capable of combining with the carboxylic ester grouping (cf. the nitration of resacetophenone, discussed by Baker, *loc. cit.*, p. 1686). (3) Owing to the uncertainty of the evidence in the aromatic series, certain dihydroxydicarboxylic esters were examined, one of which should be doubly chelated if chelation fixes a double bond in the ring, and the others only singly chelated, just as in the case of 2 : 4- and 4 : 6-diacetylresorcinols (Baker, J., 1934, 1684). The compounds prepared were *ethyl quinol-2 : 3-dicarboxylate* (VIII), ethyl quinol-2 : 5-dicarboxylate (IX), and ethyl resorcinol-4 : 6-dicarboxylate. Attempts to prepare ethyl resorcinol-2 : 4-dicarboxylate were unsuccessful. If the double bonds are fixed by chelation, then (VIII) should be

* This is actually the b. p. of the equilibrium mixture present under the particular experimental conditions, but this does not affect the reasoning which follows, as the b. p. of the pure enolic form (β-hydroxycrotonic ester) will be *lower* than this.

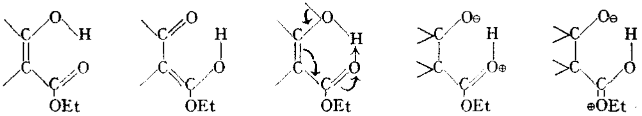
fully chelated, and (IX) and ethyl resorcinol-4 : 6-dicarboxylate incompletely chelated, which is not borne out by the depression of the m. p.'s of the substances under water :

	M. p., dry.	M. p., wet.*	Depression.
Ethyl quinol-2 : 3-dicarboxylate (VIII)	85°	68°	17°
„ „ -2 : 5- „ (IX)	133	126	7
„ resorcinol-4 : 6-dicarboxylate	140	132	8

* It was ascertained that no hydrolysis occurred during these determinations.

The evidence appears to show that (VIII), contrary to expectation, is less chelated than the other two esters.

It is difficult to explain these facts. From the behaviour of β-hydroxybutyric ester and acetoacetic ester, it seems probable that the chelate form of the latter is a resonance hybrid mainly derived from the two forms shown in the partial formulæ (X) and (XI), corresponding to the older formula (XII). Other components of the resonance hybrid



(X.) (XI.) (XII.) (XIII.) (XIV.)

not dependent upon a carbon–carbon double bond are "zwitterion" forms (XIII) and (XIV) (recalling the mechanism of the association of simple hydroxylic substances, see Sidgwick, *Ann. Reports*, 1934, **31**, 42), which, however, appear to be of little importance in the aliphatic series, but may be of greater importance in the aromatic series.

Experimental.

2-Acetyl-1-naphthol (I), prepared as described by Witt and Braun (*Ber.*, 1914, **47**, 3219) and crystallised several times from alcohol, formed very pale yellowish-green needles, m. p. 101°.

1-Acetyl-2-naphthol (II), prepared according to Fries (*Ber.*, 1921, **54**, 711) and purified by steam-distillation and finally by two crystallisations from light petroleum (b. p. 40—60°), formed almost colourless rhombic prisms, m. p. 64°.

2-Methoxy-3-naphthoic Acid.—2-Hydroxy-3-naphthoic acid (10 g.), dissolved in a mixture of acetone (100 c.c.) and water (100 c.c.), was warmed and shaken with successive small portions of methyl sulphate (in all 30 c.c.) alternately with 20% aqueous potassium hydroxide. The solution was now made strongly alkaline, heated for 2 hours on the water-bath, cooled, diluted, and acidified with hydrochloric acid. The 2-methoxy-3-naphthoic acid crystallised from dilute alcohol in pale yellow plates (9 g.), m. p. 133° (cf. Werner and Seybold, *Ber.*, 1904, **37**, 3661).

2-Methoxy-3-naphthoyl Chloride.—The foregoing acid (13·5 g.) was refluxed with thionyl chloride (60 c.c.) for 1 hour, and the product distilled, finally under diminished pressure. The acid chloride (11·5 g.), b. p. 197°/15 mm., separated from light petroleum (b. p. 60—80°) in pale yellow plates, m. p. 57° (cf. Fries and Schimmelschmidt, *Ber.*, 1925, **58**, 2839).

3-Acetyl-2-naphthol (III).—2-Methoxy-3-naphthoyl chloride was converted by the action of methylzinc iodide into 2-methoxy-3-acetylnaphthalene, and thence by demethylation with aluminium chloride into 3-acetyl-2-naphthol, following the directions of Fries and Schimmelschmidt (*loc. cit.*). The naphthol was crystallised four times from light petroleum (b. p. 60—80°) and obtained in bright yellow plates, m. p. 112°.

4-Acetyl-1-naphthol (IV).—This was prepared from α-naphthyl methyl ether *via* 1-methoxy-4-acetylnaphthalene, which was then demethylated with aluminium chloride (Witt and Braun, *loc. cit.*). It was crystallised three times from aqueous alcohol and obtained as very pale yellow needles, m. p. 197°.

1(?)-*Bromo-3-acetyl-2-naphthol.*—3-Acetyl-2-naphthol (1 g.) in glacial acetic acid (10 c.c.) was treated with a solution of bromine (2·6 g.) in acetic acid (25 c.c.). After 24 hours, the yellow crystalline powder which had separated was collected, and crystallised from acetic acid, forming bright yellow leaflets, m. p. 150° (Found, in material dried over potassium hydroxide at 100° : Br, 30·1. $C_{12}H_9O_2Br$ requires Br, 30·2%).

o-, m-, *and* p-*Hydroxybenzonitriles.*—These compounds were all prepared from the oximes

of the corresponding hydroxy-aldehydes by dehydration with acetic anhydride. The *o*-compound was crystallised from benzene–light petroleum (b. p. 60—80°), and the *m*- and the *p*-compound from carbon tetrachloride.

β-*Hydroxybutyric Ester*.—This was prepared by the catalytic hydrogenation of acetoacetic ester (Lease and McElvain, *J. Amer. Chem. Soc.*, 1933, **55**, 806), the product being freed from unchanged acetoacetic ester by shaking its ethereal solution with dilute sodium hydroxide; the solution was then dried with sodium sulphate and distilled. β-Hydroxybutyric ester gives no chelate copper derivative with copper acetate.

Ethyl Quinol-2 : 3-*dicarboxylate* (VIII).—Quinol-2 : 3-dicarboxylic acid (Thiele and Meisenheimer, *Ber.*, 1900, **33**, 675; Thiele and Günther, *Annalen*, 1906, **349**, 48) (5 g.) was refluxed for 8 hours with 3% absolute-alcoholic hydrogen chloride (100 c.c.). The bulk of the alcohol was removed by distillation, and the diluted residue, after treatment with excess of sodium bicarbonate solution, yielded to ether an oil which solidified on standing. It separated from a large volume of light petroleum (b. p. 60—80°) in needles, m. p. 85° (Found : C, 56·7; H, 5·6. $C_{12}H_{14}O_6$ requires C, 56·7; H, 5·5%).

Ethyl Quinol-2 : 5-*dicarboxylate* (IX).—This was prepared similarly from quinol-2 : 5-dicarboxylic acid (Brunner, *Annalen*, 1907, **351**, 321), and separated from alcohol in pale yellow needles, m. p. 133° (cf. Schmid, *Monatsh.*, 1911, **32**, 443).

Ethyl Resorcinol-4 : 6-*dicarboxylate*.—This ester, prepared in 35% yield in a similar manner from resorcinol-4 : 6-dicarboxylic acid, refluxing being continued for 12 hours, separated from alcohol in colourless needles, m. p. 140° (Errera, *Ber.*, 1899, **32**, 2789, gives m. p. 137°).

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107. *The Structure of Semipermeable Membranes of Inorganic Salts.*

By STANLEY FORDHAM and JOHN T. TYSON.

LITTLE seems to be known of the ultimate stiucture of semipermeable membranes of insoluble inorganic salts, although Tinker (*Proc. Roy. Soc.*, 1915, *A*, **92**, 357), from a microscopic and ultramicroscopic study, concluded that such membranes were built up of particles between 0·1 and 0·8 μ in length; he held the view, which seems to be general to-day, that they were probably amorphous. Further, Manegold (*Kolloid-Z.*, 1932, **61**, 140) gives no information as to structure, although he postulates three possible divisions according to whether the membrane is (1) canalised by polydirectional capillaries, (2) granular, as in the sand filter, or (3) sieve-like, the precipitate fibres forming the meshes.

X-Ray examination does not appear to have been applied to the study of inorganic salt membranes, no doubt owing to their thinness. It is this very feature, however, which suggests that light might be thrown on their structure by means of the method of electron diffraction.

EXPERIMENTAL.

Precipitates formed from copper sulphate, ferric chloride, or lead acetate with potassium ferrocyanide, sodium silicate, sodium tannate, or sodium hydroxide were studied, and were prepared as follows: (i) The membrane was precipitated by mixing dilute aqueous solutions of the appropriate salts, washed in distilled water, and mounted on nickel or platinum gauze, either with or without a collodion supporting film. (ii) A drop of the aqueous solution containing the acid radical was placed on a collodion film floating on a solution of the metal salt, and a current was passed between platinum electrodes immersed in the two solutions. This method worked well in the case of the ferrocyanides but not with the silicates and tannates, the ions of which were too large to be driven through the collodion films; it has been found, however, to be well suited for the preparation of films of insoluble inorganic salts with small ions. The specimens were washed by floating on several changes of distilled water. (iii) A nickel gauze was dipped into an aqueous solution of gelatin containing the metal salt, immersed when dry in a solution of the other reagent, and finally washed as before with distilled water.

The films formed by direct precipitation (i) were of necessity semipermeable, because otherwise the precipitate would clearly have grown to a dense mass. In the other cases, it was

difficult to differentiate between the permeability of the support and that of the precipitate, especially in view of the fact that flaws unresolved by a microscope with a 4 mm. dry objective may have been present.

Results.—Copper ferrocyanide. Copper ferrocyanide films prepared by any of the three methods gave patterns of which Fig. 1 is characteristic. The rings showed no tendency to arc, even when the plane of the specimen was inclined steeply to the beam; thus the crystals had no common direction of orientation. The analysis is given below (I represents the ring intensity, and d/n, calc., is the spacing, d, calculated for the simple cubic lattice, $a = 4{\cdot}98$ A., divided by the diffraction order, n), and the results agree well with a simple cubic structure; double shutter comparison (Finch and Quarrell, *Proc. Physical Soc.*, 1934, **46**, 148) with gold ($a_{Au} = 4{\cdot}070$ A.) gave $a = 4{\cdot}97_8$ A.

Copper ferrocyanide.

d/n, obs., A.	I.	Assigned indices.	d/n, calc.	d/n, obs., A.	I.	Assigned indices.	d/n, calc.	d/n, obs., A.	I.	Assigned indices.	d/n, calc.
4·99	s.	100	4·98	2·49	s.	200	2·49	1·76	v.f.	220	1·76
3·52	s.	110	3·53	2·24	f.m.	210	2·23	1·67	v.f.	300	1·66
2·88	m.	111	2·88	2·04	v.f.	211	2·04	1·57	v.f.	310	1·58

Diffraction intensities (here and in other tables): v.s. = very strong, s. = strong, m.s. = medium strong, m. = medium, f.m. = faint to medium, f. = faint, v.f. = very faint.

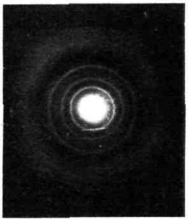
Unlike *X*-rays, electron-diffraction intensities cannot, for reasons pointed out by Finch and Sun (*Trans. Faraday Soc.*, 1935, **32**, 852), at present be utilised in carrying the analysis to the further stage of determining the position of the constituent ions. Keggin and Miles (*Nature*, 1936, **137**, 577), however, who studied by *X*-rays the structures of copper ferrocyanide, potassium ferrous ferrocyanide, Prussian-blue, and ferric ferricyanide, found in all cases a face-centred cubic structure of iron atoms with $a = 10{\cdot}2$ A. It seems reasonable to suppose that the copper ions occupy the positions midway between the iron atoms, as do the ferrous ions in ferrous ferrocyanide; in this case, since copper and iron have approximately the same scattering power for electrons, the pattern obtained would fit a simple cubic structure with a side half that of the iron lattice, *i.e.*, 5 A. This accounts for only half of the copper ions if the copper ferrocyanide contains no alkali, as is almost certain to be the case with specimens prepared by the electrolytic method. It is not possible to suggest positions for the remaining copper ions, but they cannot lie at the centres of alternate cubes of side 5 A., as do the potassium ions in Prussian-blue, since this would have given rise to diffractions of an intensity too great to have been overlooked.

In all cases the average crystal size as determined by the breadths of the diffractions was between 100 and 150 A., and in no case was evidence obtained in the form of haloes to indicate the presence of amorphous material. Tinker found with the ultramicroscope only particles between 1000 and 4000 A. in length, which he thought to be approximately spherical, but since such crystals or accumulations of crystals are much too thick to be penetrated coherently by electrons, the electron-diffraction patterns must have been obtained from other portions of the specimens. In view of the mechanical strength of copper ferrocyanide membranes, it is reasonable to assume that the larger particles are held together by the smaller particles which diffract electrons, the structure being thus similar to that found in specimens prepared by the coagulation of zinc oxide aerosols, investigated by Whytlaw-Gray, Speakman, and Campbell (*Proc. Roy. Soc.*, 1923, *A*, **102**, 600), Finch and Wilman (*J.*, 1935, 751), and Finch and Fordham (*Proc. Physical Soc.*, 1936, **48**, 85). However this may be, there can be no doubt that copper ferrocyanide membranes are either wholly crystalline or contain only a negligible proportion of amorphous material.

Copper ferrocyanide membranes formed by mixing copper sulphate and potassium ferrocyanide solutions gave specimens the colour and texture of which were independent of the concentrations and the relative proportions of the solutions. On the other hand, it was found that contact with excess potassium ferrocyanide during removal from the solution, though apparently without effect on the membrane, resulted in an electron-diffraction pattern differing from that of Fig. 1, though a few of the more intense copper ferrocyanide rings were still present. It was found that this pattern was due to the copper hydroxide described below, together with copper ferrocyanide.

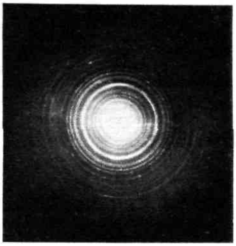
Copper ferrocyanide specimens contaminated with hydroxide (see Fig. 2) were also obtained on several occasions by the electrolytic method when a high voltage (220 volts) was used, but never with a low voltage (6—12 volts). With a high current density there was also a tendency

FIG. 1.



Copper ferrocyanide.

FIG. 2.

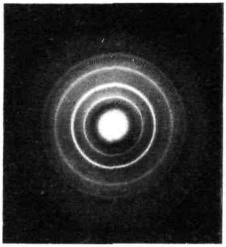


Copper hydroxide together with copper ferrocyanide.

FIG. 3.

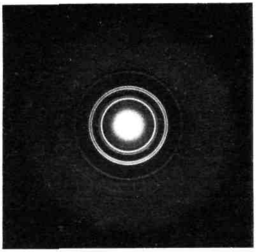
Lead ferrocyanide.

FIG. 4.



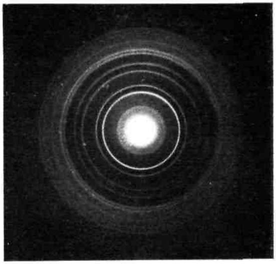
Lead silicate.

FIG. 5.



Copper hydroxide.

FIG. 6.

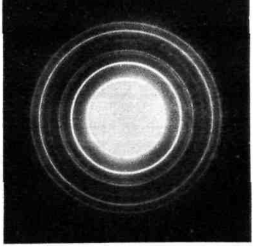


Lead hydroxide : specimen normal to the beam.

FIG. 7.

Lead hydroxide : specimen tilted.

FIG. 8.



Ferric hydroxide.

[*To face p.* **484.**

towards the formation of a blue precipitate on the upper surface of the collodion film; this was probably Prussian-blue, formed by the decomposition of the ferrocyanide ion.

Lead ferrocyanide. Lead ferrocyanide formed by the electrolytic method gave patterns similar to Fig. 3, the analysis of which is given below. The structure was simple cubic with a = 8·28 A., on which the values of d/n, calc., are based, and the crystals were greater than 200 A. in length, with no preferred direction of orientation.

Lead ferrocyanide.

d/n, obs., A.	I.	Assigned indices.	d/n, calc.	d/n, obs., A.	I.	Assigned indices.	d/n, calc.	d/n, obs., A.	I.	Assigned indices.	d/n, calc.
4·74	s.	111	4·78	2·50	s.	311	2·50	1·85	f.	420	1·85
4·17	s.	200	4·14	2·40	m.	222	2·39	1·60	f.	333	1·59
3·70	s.	210	3·70	2·08	m.	400	2·07	1·45	m.	440	1·46
3·39	m.	211	3·38	1·97	v.f.	330	1·95	1·41	m.s.	531	1·40
2·93	m.	220	2·93	1·90	v.f.	331	1·90	1·38	f.m.	600	1·38
2·82	v.f.	300	2·76								

As with copper ferrocyanide, a tendency was observed towards the formation of a hydroxide, described below, in specimens prepared both by precipitation and by electrolysis.

Ferric ferrocyanide. Ferric ferrocyanide prepared by the electrolytic method had a green colour rather than that characteristic of Prussian-blue. The patterns obtained agreed with the simple cubic structure found by Keggin and Miles to be common to several complex iron cyanides. The crystals were 150 A. in length and had no common direction of orientation.

Silicate membranes. The well-known "chemical gardens," obtained by placing a crystal of a metal salt in "water-glass" solution and commonly ascribed to the formation of membranes of metal silicates, gave in all cases patterns corresponding exactly to the hydroxide patterns described below; similar patterns were obtained from specimens prepared by precipitation from solution. It would seem that the sodium silicate in water-glass is largely decomposed into silicic acid sol and sodium hydroxide, so that the addition of a metal salt resulted in the formation of a mixed gel of the crystalline hydroxide, yielding sharp rings, and amorphous silicic acid, yielding haloes approximately coincident with those of the necessary collodion support.

The electrolytic method, in general, gave specimens consisting of the metal hydroxide, but in one case, with lead acetate, a precipitate formed on the upper surface of the collodion film and gave the pattern (Fig. 4) due to a silicate, or possibly to a different hydroxide, of lead. The plane spacings are recorded below, but no simple structure could be assigned with any certainty. The crystals were approximately 100 A. in length and had no common direction of orientation.

Lead silicate.

d/n, obs., A.	I.	d/n, obs., A.	I.	d/n, obs., A.	I.	d/n, obs., A.	I.
4·72	f.	2·19	f.	1·55	m.	1·19	v.f.
3·77	s.	1·88	m.	1·35	f.	1·10	v.v.f.
2·68	v.s.	1·75	v.v.f.	1·25	v.f.	1·02	v.f.
2·34	f.	1·67	v.v.f.				

Tannate membranes. Diffraction patterns obtained from precipitated tannate membranes consisted in all cases of three haloes somewhat similar to those afforded by amorphous substances, and almost identical with those obtained from the sodium tannate itself. Attempts to prepare tannate membranes by the electrolytic method in all cases resulted in the formation of the corresponding hydroxide.

Metal hydroxides. All the metal hydroxide specimens were prepared by the electrolytic method; dehydration might have been expected in the high vacuum of the electron-diffraction camera, but in no case was a pattern obtained which corresponded to a known oxide.

Copper hydroxide gave the pattern (Fig. 5) recorded in the table, but no simple structure could be assigned to it, nor has any X-ray work been published with which comparison could be made. The crystals were 150 A. in length and had no preferred direction of orientation.

Copper hydroxide.

d/n, obs., A.	I.	d/n, obs., A.	I.	d/n, obs., A.	I.	d/n, obs., A.	I.
5·00	f.	2·81	s.	1·75	f.	1·50	v.f.
4·10	v.s.	2·06	m.s.	1·66	f.	1·41	v.f.
3·72	m.	1·87	f.m.	1·57	v.f.	1·34	v.f.
2·99	s.						

Lead hydroxide specimens gave the pattern, Fig. 6, when normal to the beam; on tilting to 45° arcing occurred and a pattern, Fig. 7, was obtained, the analysis of which is given below. The structure was close-packed hexagonal with $a = 5{\cdot}26$ A., $c = 14{\cdot}7$ A., and $c/a = 2{\cdot}80$, on which the values of d/n, calc., are based, the c axes of the crystal being normal to the plane of the specimen. The breadths of the arcs showed that the crystals were over 200 A. in length along the a and the b axis, but probably less than 100 A. along the c axis. Lead hydroxide does not seem to have been studied by X-rays.

Lead hydroxide.

d/n, obs., A.	I.	Assigned indices.	d/n, calc.	d/n, obs., A.	I.	Assigned indices.	d/n, calc.	d/n, obs., A.	I.	Assigned indices.	d/n, calc.
4·51	f.	100	4·55	2·27	s.	200	2·28	1·73	f.m.	210	1·72
4·29	f.	101	4·35	2·16	f.n.	202	2·17	1·53	f.	300	1·52
3·68	m.s.	004	3·68	2·09	f.m.	203	2·07	1·33	f.	220	1·32
3·33	m.s.	103	3·34	1·91	m.	204	1·93	1·28	f.	310	1·27
2·65	s.	110	2·63								

Ferric hydroxide gave the pattern, Fig. 8, analysed below, the structure being face-centred cubic with $a = 5{\cdot}70$ A. The crystals were greater than 200 A. in length and had no common direction of orientation. This substance cannot be the hydroxide, goethite, Fe_2O_3,H_2O, investigated by de Jong (*Natuurwetensch. Tijds.*, 1930, **12**, 69).

Ferric hydroxide.

d/n, obs., A.	I.	Assigned indices.	d/n, calc.	d/n, obs., A.	I.	Assigned indices.	d/n, calc.	d/n, obs., A.	I.	Assigned indices.	d/n, calc.
3·26	f.	111	3·29	1·43	m.	400	1·43	0·945	f.m.	600	0·95
2·83	v.s.	200	2·85	1·31	v.f.	331	1·31	0·90	f.	620	0·90
2·00	v.s.	220	2·01	1·27	s.	420	1·27	0·86	v.f.	622	0·86
1·72	m.s.	311	1·72	1·17	m.s.	422	1·16	0·79	v.f.	640	0·79
1·64	m.s.	222	1·64	1·01	v.f.	440	1·01	0·76	v.f.	642	0·76

Discussion of Results.

The experimental results described above indicate that semipermeable membranes of different substances possess a wide variety of structures with only one feature in common, namely, that they all consist of films of gels, whether the final unit is amorphous or crystalline. The current view that semipermeable membranes are of necessity amorphous is seen to be unfounded, since all the ferrocyanide membranes examined were built up of crystals more than 100 A. in length; on the other hand, the tannate membranes were in all cases amorphous. All these membranes were normally chemically homogeneous, whereas it seems probable that silicate membranes consist of mixtures of the metal hydroxide and silicic acid gels, the former being crystalline and the latter amorphous. It seems probable that all insoluble inorganic salts would be capable of forming membranes if suitably supported, the distinguishing feature of the membranes usually employed being their mechanical strength.

The conclusions to be drawn from these results with regard to the theory of semipermeable membranes may best be discussed in the case of copper ferrocyanide. The theory put forward by Tinker depended upon a calculation of the pore size for a granular structure with particles 1000—4000 A. in diameter. The facts and considerations set forth above would seem to indicate rather a net structure, in which case no calculation of the pore size is possible. Hence, it would seem that previous evidence of a correlation between pore size and permeability is inconclusive, inasmuch as the microscope is unable to detect the presence of crystals about 150 A. in length, the presence of which in profusion must considerably modify the size of the pores. In view of the absence of other evidence in favour of a simple sieve theory of membrane action, it must be concluded that the experimental results so far published favour rather an adsorption theory as being the most likely explanation of the different permeabilities of membranes obtained from different substances by various methods of preparation.

Summary.

The structures of semipermeable membranes of the ferrocyanides, hydroxides, "silicates," and tannates of copper, lead, and tervalent iron have been examined by

electron diffraction. The ferrocyanide membranes were found to be crystalline, and whilst all the crystals exceeded 100 A. in length, many were less than 200 A.; the hydroxides were likewise crystalline. The tannates, on the other hand, were amorphous. It was found, further, that the "silicate" membranes consisted in general of mixtures of gels of crystalline metal hydroxides and amorphous silicic acid. Crystal structures are suggested for copper and lead ferrocyanides and for lead and ferric hydroxides. The results obtained show that the correlation between permeability and pore size as obtained by microscopic methods is fortuitous.

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IMPERIAL COLLEGE, LONDON, S.W. 7. [*Received, January 30th,* 1937.]

108. *The Exchange of Sulphonyl Groups.*

By D. T. GIBSON and J. D. LOUDON.

WE have independently recorded exchange of sulphonyl groups by the action of sulphinate ions on (*a*) methylthioacetonylsulphones (Gibson, J., 1932, 1819; Cowie and Gibson, J., 1933, 306; 1934, 46), (*b*) 2 : 4-dinitrodiphenylsulphones (Loudon, J., 1935, 537), and (*c*) thiolsulphonic esters (Loudon and Livingston, J., 1935, 896). The results show qualitatively that there is produced in each case an equilibrium which, it was suggested in cases (*b*) and (*c*), is chiefly determined by the relative anionic stabilities (as inferred from the strengths of the corresponding carboxylic acids) of the competing sulphonyl groups. A similar interpretation is not inconsistent with most of the data for case (*a*), except that the replacement of arylsulphonyl by alkylsulphonyl groups could not be effected. In all cases, however, in which the exchange was demonstrated, a considerable excess of the attacking ion was employed and the equilibrium point was not determined. We have now collaborated in obtaining data of a more quantitative character by measuring the change of rotation incurred by interaction with an optically active component.

Thiolsulphonic esters provided the most suitable material for investigation. Methyl camphor-10-thiolsulphonate (I) and sodium camphor-10-sulphinate (IV), having respectively $\alpha_{5461}^{19^{\circ}} = -0.53^{\circ}$ and $+0.62^{\circ}$ for $N/20$-solutions in aqueous alcohol, were selected as reference compounds and the equilibrium value for each sulphinate (II) was calculated as the percentage of the possible rotational change ($0.53^{\circ} + 0.62^{\circ} = 1.15^{\circ}$) effected by mixing $N/10$-solutions of (I) and (II) or of (III) and (IV).

$$\underset{\text{(I.)}}{C_{10}H_{15}O\cdot SO_2\cdot SMe} + \underset{\text{(II.)}}{R\cdot SO_2Na} \rightleftharpoons \underset{\text{(III.)}}{R\cdot SO_2\cdot SMe} + \underset{\text{(IV.)}}{C_{10}H_{15}O\cdot SO_2Na}$$

Although a strictly quantitative procedure was not adhered to, our results are justified by the fact that, wherever all the reactants were readily available, we were able to observe approximately the same equilibrium point by measuring both the forward and the reverse reaction and, in a test case, by actual isolation of the purified thiolsulphonic ester product in upwards of 90% of the quantity indicated. In examining a series of fourteen sulphinates, two significant points were observed: (1) The reaction proceeded so rapidly in cold aqueous alcohol that equilibrium was attained before a polarimetric reading could be taken. A similarly rapid reaction also occurred when mercaptides were employed instead of sulphinates. (2) The percentage decomposition of methyl camphor-10-thiolsulphonate increased with the various sulphinates ($R\cdot SO_2Na$) approximately as the dissociation constant for the corresponding carboxylic acid diminished. (The dissociation constants for sulphinic acids have been determined in only a few cases.) To detect any effect contributed by the SR radical, we examined 2 : 5-dichlorophenyl camphor-10-thiolsulphonate, and for solubility reasons were forced to make the comparison with the methyl ester in aqueous alcoholic dioxan solution. It will be seen (table, cols. 3 and 4) that, with the single exception of *p*-toluenesulphinate, the concordance of the values (within experimental error) suggests that the

change effected in the group SR has little influence on the equilibrium, but comparison of the values (cols. 2 and 3) resulting from modification of the solvent shows that it may be influenced by other factors.

R in $R·SO_2Na$.	Methyl camphor-10-thiolsulphonate in : aq. alcohol.	Methyl camphor-10-thiolsulphonate in : aq. alc. dioxan.	2 : 5-Dichlorophenyl camphor-10-thiolsulphonate in aq. alc. dioxan.	Dissociation constants for $R·CO_2H$ ($\times 10^{-5}$) (Beilstein).
n-Pentyl	99	100	98	1·45
Ethyl	80	—	—	1·34
p-Tolyl	78 ⇌ 27	69 ⇌ 35	77·5 ⇌ 25	4·3
p-Acetamido	70	64	61	5·17
Phenyl	68	56	55	6·6
4-Methoxy-*m*-tolyl	63 ⇌ 39	51·5 ⇌ 50	51 ⇌ 44	?
p-Fluorophenyl	54	39	41	7·39 *
α-Naphthyl	53	39	39	20·4
β-Naphthyl	43	42·5	39	6·8
p-Bromophenyl	41·5	33	31	10·8 *
p-Chlorophenyl	41	32	34	9·3
m-Nitrophenyl	11	—	8	34
o-Nitrophenyl	2	—	0	630
o-Tolyl	1	0	0	12·5
2 : 5-Dichlorophenyl	1	0	0 ⇌ 96	?

* J., 1935, 343.

The analogy which emerges between these reactions and those of the ester dismutation type is confirmed by the observation that the equilibrium

$$p\text{-}C_6H_4Me{\cdot}SO_2{\cdot}SMe + C_{10}H_{15}O{\cdot}SO_2{\cdot}S{\cdot}C_6H_3Cl_2 \rightleftarrows p\text{-}C_6H_4Me{\cdot}SO_2{\cdot}S{\cdot}C_6H_3Cl_2 + C_{10}H_{15}O{\cdot}SO_2{\cdot}SMe$$

(A.) (B.) (C.) (D.)

can be displaced either way in cold alcohol in presence of sodium acetate, C and B being isolated by using an excess of A and D respectively.

With the aid of this more sensitive optical method we confirmed that in the series (*a*) the structure $R·SO_2·CH(SAlk)·CO·CH_3$ (V) is necessary and sufficient for exchange. Thus a solution of *α*-*p*-toluenesulphonyl-*α*-methylthioacetone heated in alcohol with sodium camphorsulphinate for seventy hours at 60° showed a fall in rotation from $\alpha_{5461} - 0·5°$ to $\alpha_{5461} - 0·27°$, whereas a number of other compounds, in which not all the conditions were satisfied (experimental), showed no change. It was hoped to submit a typical compound (V) to a detailed optical investigation to clear up the discrepancy regarding exchange by aliphatic sulphinates, but in these cases exchange is so much slower that other reactions, *e.g.*, hydrolysis of acetyl, confuse the issue. It is now evident that the failure (Gibson, J., 1933, 306) to exchange arylsulphonyl for alkylsulphonyl is to be attributed not to differences in the reactivity of the sulphinates but to the incidence of hydrolysis—especially noticeable when the reagents are salts derived from relatively weaker sulphinic acids, resulting in removal of a factor ($CH_3·CO$) necessary for exchange. In former experiments the substituted acetone was specially sought as being the more significant index of the course of the reaction. We have now repeated some experiments of this type and, searching for displaced sulphinate, have shown that 2 : 5-dichlorophenylsulphonyl and 4-chlorophenylsulphonyl can be displaced by camphor-10-sulphonyl, benzylsulphonyl, and ethylsulphonyl.

The application of the method to the reaction between 10-camphor-2 : 4-dinitrophenylsulphone and sulphinates was found to be impracticable because attendant reduction processes coloured the solutions and rendered the end-point indefinite.

Experimental.

Polarimetric Procedure.—The sodium sulphinates were dried, recrystallised from alcohol, and dried. For experiments in col. 2 of the table, equal volumes of *N*/10-sulphinate in 50% alcohol

and $N/10$-methyl camphorthiolsulphonate in absolute alcohol were mixed and examined in a 1 dm. tube with mercury light (λ 5461). Reference solutions were made by diluting (*a*) $N/10$-sodium camphorsulphinate in 50% alcohol with an equal volume of absolute alcohol, and (*b*) $N/10$-methyl camphorthiolsulphonate in absolute alcohol with 50% alcohol. The solutions for cols. 3 and 4 were prepared in a similar way from the requisite volumes of $N/10$-sulphinate in 50% alcohol and $N/20$-thiolsulphonate in dioxan.

Tests for Mobility of the Sulphonyl Group (compare V above).—Phenacylphenylsulphone, α-methylsulphonyl-α-*p*-tolylthioacetone, α-tolylsulphonyl-α-2 : 5-dichlorophenylthioacetone, 4-chlorophenylsulphonylmethylthiomethane, and *p*-tolylsulphonylacetonitrile were heated severally with an alcoholic solution of sodium camphorsulphinate in sealed tubes for periods up to 40 hours. No change in rotation was observed. Solutions of sulphinate in open vessels readily undergo oxidation to sulphonate with resulting change of rotation. α-Phenylsulphonyl-α-methylthioacetone (0·2 g.) and sodium *p*-toluenesulphinate (3 g., carefully freed from carbonate), on warming with alcohol, gave α-*p*-tolylsulphonyl-α-methylthioacetone and *p*-tolylsulphonylmethylthiomethane, both identified by comparison with authentic specimens.

2 : 5-Dichlorophenyl 2 : 5-dichlorobenzenethiolsulphonate, heated in alcohol with (i) sodium camphorsulphinate, gave 2 : *5-dichlorophenyl camphorthiolsulphonate*, m. p. 121—122° (Found : Cl, 18·2. $C_{16}H_{18}O_3Cl_2S_2$ requires Cl, 18·0%); with (ii) sodium 4-chlorobenzenesulphinate, it gave 2 : *5-dichlorophenyl 4-chlorobenzenethiolsulphonate*, m. p. 121—122° (Found : Cl, 30·5. $C_{12}H_7O_2Cl_3S_2$ requires Cl, 30·2%); and with (iii) sodium 4-methoxy-*m*-toluenesulphinate, it gave 2 : *5-dichlorophenyl 4-methoxy-*m*-toluenethiolsulphonate*, m. p. 96° (Found : Cl, 19·6. $C_{14}H_{12}O_3Cl_2S_2$ requires Cl, 19·55%).

2 : *4-Dinitrophenyl-10-camphorylsulphone*, prepared from 2 : 4-dinitrochlorobenzene and sodium camphorsulphinate by heating in aqueous alcohol for 1 hour, and crystallised from alcoholic dioxan, melted at 168° and had $[\alpha]_{5461}^{18°} - 165°$ ($c = 0·97$ in dioxan) (Found : N, 7·5. $C_{16}H_{18}O_7N_2S$ requires N, 7·3%).

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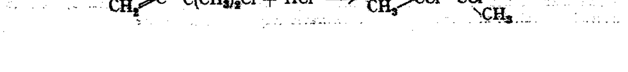
109. *The Photochemistry of Some Aliphatic Nitroso-compounds.*

By D. LL. HAMMICK and M. W. LISTER.

IN a previous communication (J., 1935, 1679) an account has been given of the photolysis of two aliphatic nitroso-compounds, nitroso*iso*propylacetone, and β-nitroso-βε-dimethylhexane, which are decomposed in benzene solution by red light with unit quantum efficiency into olefins by the elimination of the radical NOH. We have now investigated the photochemistry in solution of the following chloro- and nitro-nitroso-compounds : tetramethylethylene nitrosochloride, $CMe_2(NO)\cdot CMe_2Cl$, 1-chloro-1-nitroso*cyclo*hexane, β-chloro-β-nitroso-γγ-dimethylbutane, $CH_3\cdot CCl(NO)\cdot CMe_3$, and β-nitro-β-nitrosopropane. Schmidt (*Ber.*, 1904, **37**, 547) observed that tetramethylethylene nitrosobromide decomposes in light to give tetramethylethylene dibromide and nitric oxide. This nitroso-compound is, however, also thermally unstable, and therefore inconvenient for quantitative photochemical investigation. The corresponding nitrosochloride is, on the other hand, stable in the dark, and is decomposed in solution by red light with a quantum efficiency of about unity to give mainly tetramethylethylene dichloride, nitrogen, and nitrous acid, together with tarry material, small amounts of olefin, and hydrochloric acid. These facts make it very probable that the primary photochemical process is, as in the cases previously described, the elimination of the radical NOH and the formation of olefin, the observed production of the dichloro-derivative resulting from a series of subsequent reactions :



Most of the dimethylbutadiene is probably to be found in the gummy, intractable material.

The rate of photolysis of tetramethylethylene nitrosochloride was unaffected when the air in contact with the solutions was replaced by nitrogen or oxygen. The other nitroso-compounds investigated behaved differently. In the dark they were stable in the presence of oxygen, but on illumination in various solvents they underwent photo-oxidation with low quantum efficiencies to the corresponding nitro-compounds.

EXPERIMENTAL.

Preparation of Materials.—Tetramethylethylene nitrosochloride was prepared as described by Thiele (*Ber.*, 1894, **27**, 455); m. p. 121°.

1-Chloro-1-nitroso*cyclo*hexane has been prepared by Rheinboldt (*Annalen*, 1927, **455**, 300) by the action of nitrosyl chloride on *cyclo*hexanoneoxime. The following preparation is more convenient: 10 g. of *cyclo*hexanoneoxime were dissolved in dilute hydrochloric acid and cooled in ice. A fairly rapid stream of chlorine was passed through the solution until no more gas was absorbed. The blue oil that separated was taken up in ether, and washed with sodium bicarbonate solution and with water. After drying with anhydrous sodium sulphate, the ether was removed; the nitroso-compound distilled under diminished pressure as a purple oil with a very unpleasant smell, b. p. 58—59°/13 mm.

β-Chloro-β-nitroso-γγ-dimethylbutane, prepared from pinacolinoxime by a process exactly similar to that described above for chloronitroso*cyclo*hexane, formed very volatile, bright blue, diamond-shaped crystals, m. p. 119° (Rheinboldt, *loc. cit.*).

β-Nitro-β-nitrosopropane was prepared by a modification of Schmidt's method (*Ber.*, 1900, **33**, 875): 3·5 g. of acetoneoxime in 100 c.c. of ether were added to 10 g. of sodium nitrite in 50 c.c. of water, and the whole cooled in a freezing mixture. 24 G. of a 30% (by weight) solution of sulphuric acid in water were run in slowly with shaking, so that the ψ-nitrole was taken up in the ethereal layer as soon as it was produced. The ethereal solution was washed and dried as for 1-chloro-1-nitroso*cyclo*hexane, and finally distilled with a short fractionating column (owing to the volatility of the nitroso-compound) until colourless crystals appeared; m. p., after washing with cold dry ether, 76° (cf. Schmidt, *loc. cit.*).

Tetramethylethylene nitrosobromide and α-chloro-α-nitrosoethylbenzene were also prepared by analogous methods, but owing to their thermal instability their photo-kinetics were not investigated. It was found possible, however, by working rapidly to determine their absorption spectra in solution.

Molecular Weights.—The molecular weight of each nitroso-compound was determined cryoscopically in benzene and found either to be unimolecular (blue solids) or to diminish, after various lengths of time, in the way characteristic of aliphatic nitroso-compounds (colourless in the solid state) to a steady value corresponding to the unimolecular form. We quote one example:

0·1500 G. of β-nitro-β-nitrosopropane ($C_3H_6O_3N_2$ = 118) in 15·495 g. of benzene.

Time	35 mins.	115 mins.	15 hours
Depression of f. p.	0·340°	0·408°	0·434°
M	147·3	122·8	115·4

Absorption Spectra.—Preliminary experiments with all the nitroso-compounds investigated except tetramethylethylene nitrosobromide and α-chloro-α-nitrosoethylbenzene showed that Beer's law was obeyed in each of the solvents used in the photokinetic experiments. Colour densities D were determined in a 2-cm. absorption tube, with benzene solutions that had been allowed, in the cases of the thermally stable compounds, to stand overnight to ensure complete dissociation to the unimolecular forms. Data are in Table I. The extinction coefficient ε is defined by the relation $I_{\text{transmitted}}/I_{\text{incident}} = 10^{-\varepsilon cl} = 10^{-D}$; c is concentration in g.-mols./l. in a tube of length l cm.

Photokinetics.—*Apparatus.* The optical system used directed a parallel beam of light (diam., 2·7 cm.) from a 1500-watt filament lamp into the photo-cell (diam. 5·5 cm., thickness 1·0 cm., capacity about 25 c.c.). The voltage across the filament was maintained constant, and the radiation from the lamp showed no appreciable change, as measured with a thermopile, throughout the series of experiments. Owing to the fact that no colour filters are known that will transmit even approximately monochromatic light at wave-lengths within the range of those absorbed by the nitroso-compounds investigated, the only filter used was one to eliminate infra-red radiation.*

* The filter solution contained 18 g. of $NiCl_2,6H_2O$, 50 g. of $FeSO_4,(NH_4)_2SO_4,6H_2O$, 6 c.c. of concentrated hydrochloric acid, and 3 c.c. of concentrated sulphuric acid per litre.

TABLE I.

Tetramethylethylene nitrosochloride.

λ	7500	7400	7300	7200	7100	7000	6900	6800	6700
ϵ	2·67	5·25	7·89	11·03	14·71	17·65	17·94	17·35	15·64
λ	6600	6500	6400	6300	6200	6100	6000	5800	5500
ϵ	12·75	10·30	8·68	7·59	6·45	5·15	4·01	2·45	1·03

$\epsilon_{max.}$ = 17·94 at 6900 A.

1-*Chloro*-1-*nitroso*cyclo*hexane.*

λ	7500	7400	7300	7200	7100	7000	6900	6800	6700	6600
ϵ	0·60	0·99	1·44	2·32	3·78	5·87	8·15	10·77	14·53	17·27
λ	6500	6400	6300	6200	6100	6000	5900	5800	5700	5600
ϵ	17·60	15·93	12·73	10·70	9·10	6·40	4·29	2·73	1·27	0·67

$\epsilon_{max.}$ = 17·87 at 6550 A.

β-*Chloro*-β-*nitroso*-γγ-*dimethylbutane.*

λ	7400	7300	7200	7100	7000	6900	6800	6700
ϵ	1·50	2·01	3·31	4·85	7·15	10·51	14·63	17·10
λ	6600	6500	6400	6300	6200	6100	6000	
ϵ	16·18	13·38	10·51	9·57	8·35	7·29	5·83	

$\epsilon_{max.}$ = 17·10 at 6700 A.

β-*Nitro*-β-*nitrosopropane.*

λ	7500	7400	7300	7200	7100	6900	6800	6700	6600
ϵ	0·02	0·58	1·12	1·60	3·47	6·52	12·41	17·31	19·92
λ	6550	6500	6400	6300	6200	6100	6000	5900	5500
ϵ	21·29	21·04	18·39	16·67	14·42	12·43	10·03	8·60	3·69

$\epsilon_{max.}$ = 21·29 at 6550 A.

Tetramethylethylene nitrosobromide.

λ	7500	7400	7300	7200	7100	7000
ϵ	1·15	4·26	6·71	11·43	15·14	17·11
λ	6900	6800	6700	6500	6400	6000
ϵ	17·76	16·16	12·88	8·57	5·66	2·58

$\epsilon_{max.}$ = 17·76 at 6900 A.

α-*Chloro*-α-*nitrosoethylbenzene.*

λ	7500	7400	7300	7200	7100	7000	6900	6800	6700
ϵ	0·44	0·78	1·23	1·60	2·48	3·66	4·94	8·42	11·77
λ	6500	6400	6300	6200	6100	6000	5900	5700	5500
ϵ	17·02	16·34	14·38	11·83	9·23	9·31	7·33	5·22	2·74

$\epsilon_{max.}$ = 17·02 at 6500 A.

The photo-cell contained a small piece of soft iron enclosed in glass, and was stirred by an electromagnetic device.

Solutions of the nitroso-compounds were made up in the various solvents so that their colour densities at the maximum of absorption were about 2, for at such concentrations the fraction of light absorbed is nearly 100% and changes only slowly with concentration. All solutions were kept in the dark for a time sufficient to ensure that dissociation into the unimolecular form was complete. The rate of disappearance of the blue nitroso-molecules when irradiated was followed by measurements of colour densities at some convenient wave-length with the Hilger–Nutting spectrophotometer.

In each case the relation between rate of photolysis and light intensity was determined directly by the interposition of a metal gauze in the irradiating beam of light, the ratio of light transmitted to that incident upon it being determined with a thermopile.

Lastly, the quantum efficiencies of the photochemical processes were found from a comparison of the mean amount of energy absorbed per minute by a solution as measured with the thermopile, and the number of g.-mols. of nitroso-compound destroyed per minute. Owing to the fact that all the nitroso-compounds investigated were found to obey Beer's law, the latter rate is given by $k = n\left(\frac{D_0 - D_1}{D_0}\right)\frac{1}{\partial T}$, where n = number of g.-mols. of nitroso-compound initially present in the photo-cell, D_0 is the initial colour density, and D_1 that after an interval of T

minutes. In all cases the mean value of $(D_0 - D_1)/\partial T$ was taken as that given by the slope of the straight-line plot of colour density against time.

We give our data for the photolysis of tetramethylethylene nitrosochloride in contact with air in some detail in order to indicate the kind of concordance attained, the number of measurements made, etc., in all our experiments, the results of which are summarised in Table II.

Tetramethylethylene nitrosochloride.

c = 0·5355 g. in 19·48 g. of benzene.

Time (mins.)	0	15	25	40	55
(i) D_{6700}	2·21	2·11	2·04	1·955	1·865
(ii) D_{6500}	1·540	1·465	1·420	1·363	1·310

These data give satisfactory plots of D against T, from which

$$\left.\begin{array}{l}\text{rate (i)} = 1{\cdot}02 \times 10^{-5}\text{ g.-mol./min.}\\ \text{rate (ii)} = 0{\cdot}97 \times 10^{-5}\quad ,,\end{array}\right\}\text{mean } 1{\cdot}00 \times 10^{-5}\text{ g.-mol./min.}$$

A piece of metal gauze was now interposed between the light source and the photo cell.

0·3832 G. of nitroso-compound in 18·90 g. of benzene.

Time (mins.)	0	30	60	90	120
D_{6700}	1·714	1·631	1·555	1·468	1·385

From the plot, which is a straight line, of D against T, the rate of photodecomposition is $0{\cdot}41 \times 10^{-5}$ g.-mol./min.; the ratio of transmitted to incident light, found with the thermopile, was 0·41. The rate of photolysis is thus proportional to the first power of the light intensity.

Quantum efficiency. Measurements with the thermopile showed that the mean absorption of energy during the run referred to above (no gauze present) was 0·391 cal./min., which leads to a quantum efficiency of very nearly unity (1·04) on the assumption that the mean frequency of the absorbed radiation is that of the wave-length at maximum absorption (6900 A.).

TABLE II.

Quantum efficiencies.

Substance.	Solvent. C_6H_6.	CHCl$_3$.	MeOH.	EtOH.
Tetramethylethylene nitrosochloride	1·04	0·84	1·94	1·87
β-Chloro-β-nitroso-γγ-dimethylbutane	0·91	0·93	1·75	1·56
Chloronitroso*cyclo*hexane	0·81	—	2·42	2·17
β-Nitro-β-nitrosopropane	0·82	0·85	—	—

The above data show that the photolysis in contact with air of the four nitroso-compounds resembles quantitatively that of the nitroso-derivatives previously investigated (*loc. cit.*) in that the quantum efficiencies are in the neighbourhood of unity. The solvent influence which can cause a 2—3-fold variation in the apparent quantum efficiency is of the type already well known (Moelwyn-Hughes, " Kinetics of Reactions in Solution," pp. 71, 155).

Photo-oxidation.—The effect of oxygen on the photolysis of the nitroso-compounds was investigated by making successive determinations of the velocity of photo-reaction at constant light intensity with the solution in contact with nitrogen, air, or oxygen. The results are in Table III. Owing to the high volatility of the nitroso-compounds, it was found impossible effectively to " boil out " the solutions in contact with pure nitrogen or oxygen. The space above the solutions was therefore swept out as thoroughly as possible with these gases.

TABLE III.

Rate of photo-reaction at constant illumination (g.-mols./min. × 10^{-5}).

Substance.	Solvent.	Nitrogen.	Air.	Oxygen.
Tetramethylethylene nitrosochloride	C_6H_6	1·08	1·04	1·06
	MeOH	2·41	2·41	2·57
β-Chloro-β-nitroso-γγ-dimethylbutane	C_6H_6	<0·2	0·87	1·71
	MeOH	0·81	1·67	2·41
Chloronitroso*cyclo*hexane	MeOH	2·22	3·25	—
β-Nitro-β-nitrosopropane	C_6H_6	<0·3	0·82	0·89

The above figures show that the photolysis of tetramethylethylene nitrosochloride is unaffected by the presence or absence of oxygen. In the three other cases, however, the results

indicate that a photo-oxidation of some kind occurs; an indication as to the nature of this oxidation is given by an examination of the products of the photo-reaction.

Products of the Photo-reactions.—*Tetramethylethylene nitrosochloride.* Benzene solutions, illuminated in either presence or absence of air, evolved a gas, identified as nitrogen, and ultimately became colourless. An aqueous extract of the solution was found to contain nitrous acid and traces of hydrochloric acid. The benzene was found to contain tetramethylethylene dichloride, $CMe_2Cl\cdot CMe_2Cl$, m. p. and mixed m. p. 160°. An intractable gummy material, together with some unsaturated substance (reaction with bromine), was also present.

β-Chloro-β-nitroso-γγ-dimethylbutane. Solutions in benzene or ethyl or methyl alcohol gave, on illumination in contact with air, the corresponding nitro-compound, m. p. and mixed m. p. 166°. In absence of air, very little photolysis occurred, even after prolonged irradiation.

1-*Chloro*-1-*nitroso*cyclo*hexane.* The illumination of a benzene solution of this substance resulted in the separation of a gummy material (this fact prevented the measurement of photokinetics in benzene solution). Separation did not occur in alcoholic solution, from which on dilution with water an oil separated. This, after drying in ether, distilled at 90°/13 mm.; this b. p. was unaffected by the addition of authentic chloronitro*cyclo*hexane. The main reaction is thus an oxidation of the nitroso- to the nitro-group. Traces of nitrous acid and hydrochloric acid indicated that the photo-oxidation is not the only reaction that occurs. This was confirmed by the exposure of a solution in ether to light, air being excluded. The nitroso-compound was ultimately transformed into a brown, insoluble, gummy material, with small quantities of nitrous and hydrochloric acids. No gaseous products were observed.

β-Nitro-β-nitrosopropane. Photo-oxidation in benzene yielded mainly ββ-dinitropropane (m. p. and mixed m. p. 53°). Photolysis occurred to some extent in absence of air, nitrogen being evolved; a satisfactory isolation of other products has, however, not yet been achieved.

Summary and Observations.

The aliphatic nitroso-compounds studied in the course of this and of the previous investigation (Anderson, Crumpler, and Hammick, J., 1935, 1679) resemble one another very closely in the way in which their solutions absorb light. The nearly symmetrical absorption curves are very similar in shape and are very little affected by change of solvent. Values for the extinction coefficients at the maximum of absorption in benzene are collected below, and show how little considerable variation in molecular weight and structure affects absorptive power.

Substance.	ε.	Substance.	ε.
Nitroso*iso*propylacetone	24·3	β-Nitroso-βε-dimethylhexane	20·0
Tetramethylethylene nitrosochloride	17·9	1-Chloro-1-nitroso*cyclo*hexane	17·9
Tetramethylethylene nitrosobromide	17·7	β-Nitro-β-nitrosopropane	17·1
β-Chloro-β-nitroso-γγ-dimethylbutane	17·1	α-Chloro-α-nitrosoethylbenzene	17·0

Although the molecules of these nitroso-compounds can all absorb very nearly the same amount of light energy by means of the nitroso-group, however, it is now clear that the activated molecule can behave in different ways depending on its structure and composition. First, we have the behaviour of nitroso*iso*propylacetone, β-nitroso-βε-dimethylhexane and, if our interpretation of its photochemistry is accepted, tetramethylethylene nitrosochloride; these substances on the absorption of 1 quantum of light energy eliminate the radical NOH in either the presence or absence of oxygen. Secondly, it appears from the examples so far examined that, if the carbon atom to which the nitroso-group is attached is also linked to an atom other than carbon (halogen or the nitro-group), then in the presence of oxygen a light-catalysed oxidation occurs with roughly unit quantum efficiency. In the absence of oxygen, these nitroso-compounds undergo photochemical decomposition to a greater or less extent. β-Chloro-β-nitroso-γγ-dimethylbutane and β-nitro-β-nitrosopropane appear slowly to eliminate NOH as in the case of the non-photo-oxidisable compounds. 1-Chloro-1-nitroso*cyclo*hexane undergoes a comparatively rapid photo-reaction that does not involve oxygen; practically no gas is evolved in the course of its transformation into the intractable material which is the only product that we have so far been able to isolate.

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The Dyson Perrins Laboratory, Oxford University. [*Received, January 13th*, 1937.]

NOTES.

Glucovanillin and a Colour Reaction for Vanillin. By WILLIAM V. THORPE and R. TECWYN WILLIAMS.

HELFERICH and SCHMITZ-HILLEBRECHT (*Ber.*, 1933, **66**, 378) have shown (and we have confirmed) that, whereas phenyl-β-glucoside can be prepared by condensing phenol with β-penta-acetyl glucose in the presence of *p*-toluenesulphonic acid, phenyl-α-glucoside results if anhydrous zinc chloride is used as catalyst. When this method was applied to prepare the vanillin glucosides, with either catalyst, the only crystalline product isolated was tetra-acetyl vanillin-β-glucoside. The procedure used by Helferich and Schmitz-Hillebrecht was followed exactly in both cases, vanillin being used instead of phenol. The tetra-acetyl vanillin-β-glucoside (cf. Fischer and Raske, *Ber.*, 1909, **42**, 1465), recrystallised from aqueous alcohol, had m. p. 142—143°, $[\alpha]_D - 48.3°$ ($c = 1$ in chloroform) (Found: OMe, 6·5. Calc. for $C_{22}H_{26}O_{12}$: OMe, 6·4%). The 2 : 4-*dinitrophenylhydrazone* crystallised from pyridine–ligroin in orange needles, m. p. 202—203° (Found: OMe, 4·7. $C_{28}H_{30}O_{15}N_4$ requires OMe, 4·7%).

The tetra-acetate was deacetylated by sodium methoxide in methyl alcohol (cf. Bergmann and Heimhold, J., 1936, 505); the resulting vanillin-β-glucoside (β-glucovanillin) (Fischer and Raske, *loc. cit.*), recrystallised from methyl alcohol, formed long, very fine needles, m. p. 189—190°, $[\alpha]_D^{21°} - 86.6°$ ($c = 0.72$ in water) (Found: OMe, 10·1. Calc. for $C_{14}H_{18}O_8$: OMe, 9·9%). The 2 : 4-*dinitrophenylhydrazone* crystallised from dioxan–ligroin in rust-red needles, m. p. 260—264° (Found: OMe, 6·0. $C_{20}H_{22}O_{11}N_4$ requires OMe, 6·3%).

Colour Reaction of Vanillin.—When 1 c.c. of an aqueous solution of vanillin is boiled with two drops of Millon's reagent, a characteristic stable purple colour (or precipitate with concentrated solutions) is obtained. The reaction seems specific for the vanillin group in that, out of 63 phenols examined (including eugenol, *iso*eugenol, guaiacol, and protocatechuic aldehyde and acid), only vanillin and vanillic acid gave the colour immediately. The reaction is given after longer boiling by acetylvanillin, β-glucovanillin, and potassium glucurovanillate. *iso*Eugenol with *excess* of reagent gives a fugitive purple colour turning to brown. *p*-Aminophenol gives a very transient purple turning to deep red.

The reaction is positive with a 0·002% vanillin solution. In very dilute solutions the mixture must stand for a few minutes to develop the maximum colour. With an excess of reagent, as with other phenols, no colour is obtained. 5-Nitrovanillin gives no reaction (cf. *o*-, *m*-, and *p*-nitrophenols and picric acid, which give no colour with Millon's reagent). The reaction is not given with the separated or paired constituents of Millon's reagent.—UNIVERSITY OF BIRMINGHAM. [*Received, December 10th*, 1936.]

Some Pyrimidine Derivatives. By A. BOWMAN.

THE following new pyrimidine derivatives were prepared by adaptations of known methods during an investigation which was not pursued owing to the appearance of publications (Bergel and Todd, *Nature*, 1936, **138**, 76, 406; Williams and Cline, *J. Amer. Chem. Soc.*, 1936, **58**, 1504), dealing in part with the same topics.

2 : 4 : 6-*Trimethylpyrimidine Dihydrate.*—Acetylacetone (11 g.) was added to a solution of acetamidine hydrochloride (10 g.) ("Organic Syntheses," VIII, 1) and potassium carbonate (28 g.) in water (95 c.c.). After 2—3 weeks the crystalline mass was collected, washed with a little cold water, and dried; evaporation of the mother-liquor gave a further crop (total yield, 3·8 g.). The *compound* separated from water or ether in long, colourless, filiform needles, m. p. 47—48°; it sublimed unchanged in a vacuum at 30—40° and had a strong odour of crude acetamide (Found: C, 53·0; H, 8·7; N, 17·4. $C_7H_{10}N_2,2H_2O$ requires C, 53·1; H, 8·9; N, 17·7%). Dehydration took place above the m. p.

2 : 4 : 6-*Trimethylpyrimidine.*—From the mother-liquor of the above preparation, saturated with potassium carbonate, ether extracted a yellowish oil (1 g.), b. p. 160° (approx.), which absorbed moisture from the air and solidified to crystals of the dihydrate. Aqueous solutions of both the base and the dihydrate yielded with mercuric chloride a sparingly soluble double *compound*, m. p. 169° after sintering at 164° (Found: Cl, 21·2. $C_7H_{10}N_2,2HgCl_2$ requires Cl, 21·3%).

2 : 4 : 6-*Tristyrylpyrimidine.*—2 : 4 : 6-Trimethylpyrimidine dihydrate (0·8 g.) was heated for 3—4 hours at 150° with an excess of benzaldehyde (4 g.) and a trace of anhydrous zinc

chloride. Excess of benzaldehyde was removed by steam-distillation and the residual brown solid was washed successively with water, alcohol, and a little cold benzene, and then dried (yield, 1·4 g.). The *compound* crystallised in microscopic colourless needles from benzene and was faintly yellow in bulk; m. p. 198—199° (Found: C, 87·1; H, 5·8; N, 7·2. $C_{28}H_{22}N_2$ requires C, 87·0; H, 5·7; N, 7·2%).

2-Phenylpyrimidine-4 : 6-dicarboxylic Acid.—2-Phenyl-4 : 6-dimethylpyrimidine (3 g.) (Pinner, *Ber.*, 1893, **26**, 2125) was heated for 12 hours under reflux with 1% potassium permanganate solution (1050 c.c.). The filtered solution after evaporation to small bulk (75 c.c.) was acidified with dilute hydrochloric acid and the precipitated white crystalline powder was collected, recrystallised from aqueous alcohol, and dried at 110°. The *acid* began to decompose at 165° and subsequently melted at a temperature depending on the rate of heating (Found: C, 59·1; H, 3·5; N, 11·5. $C_{12}H_8O_4N_2$ requires C, 59·0; H, 3·3; N, 11·5%).

2-Phenyl-4-methylpyrimidine-6-carboxylic Acid.—Oxidation of 2-phenyl-4 : 6-dimethylpyrimidine (5·5 g.) in boiling water (500 c.c.) by dropwise addition of aqueous potassium permanganate (9·5 g. in 500 c.c.) and fractional acidification of the concentrated filtrate from the reaction gave, in addition to the dibasic acid described above, the monobasic *acid* (0·7 g.), m.p. 112° (decomp.) (Found: C, 67·1; H, 4·9. $C_{12}H_{10}O_2N_2$ requires C, 67·3; H, 4·7%). Unchanged initial material (2·7 g.) was recovered.

2 : 4-Dichloro-5-chloromethyl-6-methylpyrimidine.—4-Methyl-5-hydroxymethyluracil (8 g.) (Kircher, *Annalen*, 1911, **385**, 293) and phosphorus oxychloride (80 c.c.) were heated on the water-bath for 8 hours. After removal of the excess of phosphorus oxychloride in a vacuum the residual oil was poured on ice; it solidified on standing. The yellowish-white solid was dissolved in a little alcohol and reprecipitated from the filtered solution by water (yield, 7·6 g.; 70%). The compound separated from light petroleum in large colourless prisms, m. p. 38—39° (Found: C, 34·1; H, 2·3; N, 13·3; Cl, 50·2. Calc. for $C_6H_5N_2Cl_3$: C, 34·0; H, 2·4; N, 13·2; Cl, 50·4%). Todd *et al.* (J., 1936, 1604) obtained a 37% yield and record m. p. 38—39°.

3-(2′ : 4′-Dichloro-6′-methylpyrimidyl-5′-methyl)-5-β-hydroxyethyl-4-methylthiazolium Chloride.—5-β-Hydroxyethyl-4-methylthiazole (104 mg.) (Buchman, *J. Amer. Chem. Soc.*, 1936, **58**, 1803) was heated for 24 hours at 60—65° with 2 : 4-dichloro-5-chloromethyl-6-methylpyrimidine (154 mg.) and absolute methyl alcohol (0·05 c.c.). The cooled product, washed with a little cold absolute alcohol and recrystallised by addition of ether to a warm solution in absolute alcohol (yield, 48 mg.), formed irregular, faintly yellow plates, m. p. 202·5° after sintering at 201° (Found: C, 41·2; H, 4·3; N, 11·9; Cl, 30·0. $C_{12}H_{14}ON_3Cl_3S$ requires C, 40·6; H, 4·0; N, 11·9; Cl, 30·0%). The *chloride* showed in alcoholic solution a blue fluorescence in ultra-violet light, and gave a positive formaldehyde-azo test (Kinnersley and Peters, *Biochem. J.*, 1934, **28**, 667). By the catatorulin test (Passmore, Peters, and Sinclair, *ibid.*, 1933, **27**, 842; Peters, *ibid.*, 1935, **29**, 712) no aneurin activity was shown.

The author thanks Professor R. Robinson, F.R.S., for his interest in the work, Professor R. A. Peters, F.R.S., for the biological examination of specimens, and Dr. E. R. Buchman for a gift of 5-β-hydroxyethyl-4-methylthiazole.—Dyson Perrins Laboratory, Oxford University. [*Received, December 10th*, 1936.]

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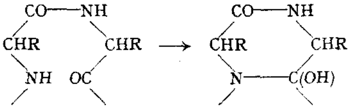
110. *The Association of α-Piperidone.*

By G. I. Jenkins and T. W. J. Taylor.

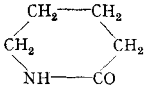
It is becoming increasingly probable that a simple protein should be regarded as consisting essentially of a polypeptide chain folded into some characteristic pattern and held in that arrangement by links between certain points of the chain, and that denaturation of the protein, and possibly also its spreading as a film on a water surface, is a result of an unfolding to give a chain which is not characterised by one particular arrangement of the parts (Wrinch, *Nature*, 1936, **137**, 411; Mirsky and Pauling, *Proc. Nat. Acad. Sci.*, 1936, **22**, 439). Two suggestions have been made as to the nature of the linkages between the groups of the polypeptide chain. The first is a kind of ring-chain tautomerism, in which spatially suitable imino- and carbonyl groups are involved, and it has been pointed out that this could lead to

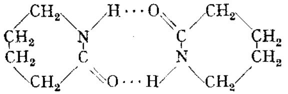
polycyclic folding of the chain (Wrinch, *loc. cit.*; *Nature*, 1936, **138**, 241). In a simple case it can be formulated as follows:

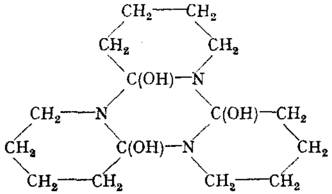


In the second suggestion, the essential mechanism is taken to be hydrogen-bond formation between the same groups and also, possibly, between free amino- and carboxyl groups carried on side chains (Mirsky and Pauling, *loc. cit.*). The two views have been combined in the suggestion that polycyclic assemblies formed in the first manner might associate further by hydrogen-bond formation (Wrinch and Jordan-Lloyd, *Nature*, 1936, **138**, 758).

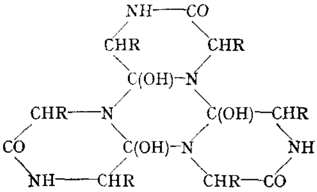
As a consequence of these views, it seemed of interest to establish the type of association in the simple cyclic imide α-piperidone (I), in which the peptide linking –NH–CO– already forms part of a ring. If, as in the first suggestion, there is a tendency for the building up of polycyclic systems, the compound might associate to the trimeric form (II), the structure of which would be very similar to that which Wrinch has postulated as a possible form of a cyclic hexapeptide (III). If, on the other hand, association takes place by hydrogen-bond formation, the polymerised form would presumably be dimeric, with the structure (IV), which is analogous to that of the dimeric form of a carboxylic acid.

(I.) 

 (IV.)



(II.)



(III.)

A trimeric form held together by hydrogen bonds is unlikely; it would contain what would amount to a nine-membered ring, which, because of its small probability of formation, could hardly be present in appreciable quantity in equilibrium with the dimeric and monomeric forms.

The apparent molecular weight of α-piperidone in solution in benzene and in water has been measured by the cryoscopic method. In water the compound shows practically no sign of association at all, presumably because the peptide group is combined with the solvent. In benzene, on the other hand, even at low dilution, the apparent molecular weight is 1·75 times the formula weight, and, as the concentration increases, approaches a value twice that of the formula weight. There is no indication of the existence of a trimeric complex.

The association of several simple amides and anilides has been determined by Meldrum and Turner (J., 1908, **93**, 876) by the boiling-point method. They found practically no indication of association in water, alcohol, or acetone, except possibly with benzamide. Nearly all the compounds were associated in benzene and chloroform. Thus, in general, the behaviour of the cyclic imide resembles that of the amides, and there is the same instability

in water of the hydrogen bonds necessary for association. Direct comparison of the boiling-point results with ours is impossible because of the temperature difference, but the amides do not appear to give dimeric molecules at such low concentrations as piperidone does.

EXPERIMENTAL.

α-Piperidone was prepared by the Beckmann rearrangement of *cyclo*pentanoneoxime (Wallach, *Annalen*, 1900, **312**, 179). It is extremely hygroscopic, and was dried by dissolving it in benzene and removing the solvent in a stream of dry air. It was finally distilled under reduced pressure (b. p. 134—137°/11 mm.), and collected in a glass tube of 7 mm. bore. The rod of solid thus obtained was cut into pellets of suitable size, which were kept in a vacuum over calcium chloride. Freezing-point measurements were made by the ordinary Beckmann method; with benzene as solvent a counter-current of dried air prevented the access of moisture. The benzene was of AnalaR quality, further purified by freezing out, and dried with and distilled from phosphoric oxide in an all-glass apparatus in dry air; its f. p. constant was found to be 52·34° per g.-mol. per 100 g. of solvent, pure naphthalene being used as solute. With both solvents and with all solutions, the amount of supercooling was kept to 0·8° as closely as possible; the aqueous solutions had to be seeded with a small crystal of ice.

α-Piperidone in benzene (formula weight = 99·1).				α-Piperidone in water.			
Piperidone, mols. %.	Δ.	Apparent mol. wt.	Assoctn. factor.	Piperidone, mols. %.	Δ.	Apparent mol. wt.	Assoctn. factor.
1·421	0·564°	169·8	1·71	0·699	0·720°	100·1	1·01
2·666	1·019	178·6	1·80	1·117	1·130	102·3	1·03
5·142	1·944	185·3	1·87	1·786	1·770	105·1	1·06
7·460	2·825	189·6	1·91	2·471	2·423	106·9	1·08
				3·671	3·575	109·1	1·10

We express our thanks to Dr. D. Wrinch, who suggested the measurements to us, and to the Rockefeller Foundation for a grant.

THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, February 9th*, 1937.]

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111. *Sumatrol. Part I.*

By ALEXANDER ROBERTSON and GEORGE L. RUSBY.

IN the course of an examination of a resin obtained from a species of *Derris* (probably *Derris malaccenis*, var. *Sarawakenis*; compare Henderson, *Malayan Agric. J.*, 1934, **22**, 125) rich in toxicarol, Cahn and Boam (*J. Soc. Chem. Ind.*, 1935, **54**, 42T) isolated in small amount (0·55% of crude resin) a new colourless crystalline compound which appeared to be dimorphic, m. p. 189° and m. p. 192—194°, and which they considered to have the empirical formula $C_{23}H_{22}O_7$, although their analytical results did not exclude the formula $C_{20}H_{20}O_6$. This substance, which, on the basis of the former formula, is isomeric with tephrosin and toxicarol, gave a strong ferric reaction, could not be dehydrated by means of a mixture of acetic acid and sulphuric acid, and gave a liquid product on treatment with acetylating agents. Preliminary tests indicated that, like other derris constituents, the new compound had insecticidal properties. Through the kindness of Dr. R. S. Cahn and of Messrs. Cooper, McDougall, and Robertson, Ltd., of London, in placing a supply of the resin at our disposal we have been able to make a detailed examination of the new compound, which has now been named *sumatrol* (private communication from Dr. Cahn).

Sumatrol was isolated from the resin according to the procedure employed by Cahn and Boam (*loc. cit.*), but the melting point phenomena observed by us are not quite identical with those previously reported (see experimental section). Until a detailed crystallographic examination of the forms, m. p. 189° and m. p. 194° (Cahn and Boam, *loc. cit.*, and present work), is available it is impossible to say whether the results obtained are due to solvents of crystallisation or to the existence of dimorphic forms, but it may be noted that similar properties are exhibited by a surprisingly large number of members of the rotenone group, where in some cases the existence of dimorphic forms has been clearly established (compare

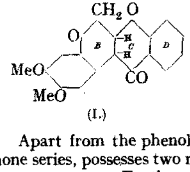
La Forge and Keenan, *J. Amer. Chem. Soc.*, **1931**, **53**, 4450; Gooden and Smith, *ibid.*, **1935**, **57**, 2616). The analytical results obtained for sumatrol, together with those of certain derivatives subsequently discussed, clearly show that the compound has the formula $C_{21}H_{16}O_5(OMe)_2$ and is thus isomeric with tephrosin and toxicarol as Cahn and Boam suggested (*loc. cit.*). We have also confirmed the observations of these workers that, unlike tephrosin, sumatrol cannot be dehydrated. The formation of an *oxime* establishes the presence of an active carbonyl group, and this fact, in conjunction with the strong ferric reaction, clearly indicates that there is a phenolic hydroxyl group in the *o*-position to the carbonyl group; in agreement with this conclusion it has been observed that, like toxicarol, sumatrol is almost insoluble in aqueous sodium hydroxide. Acetylation of sumatrol gave rise to an amorphous product, which has not yet been obtained crystalline and has a negative ferric reaction; this product may be the monoacetate, the diacetate derived from an enolic form, or, more probably, a mixture of both.

Whilst the oxidation of sumatrol with potassium ferricyanide did not appear to proceed smoothly, treatment of the compound with iodine and sodium acetate and elimination of iodine from the product by means of zinc dust and acetic acid according to the standard procedure gave rise to *dehydrosumatrol* which, like the parent compound, is optically active, is almost insoluble in dilute aqueous sodium hydroxide, and gives a strong ferric reaction. As in the case of sumatrol itself, the last two properties indicate that the dehydro-derivative contains a phenolic group in the *o*-position to a carbonyl group, and the presence of this hydroxyl group in the dehydro-compound and hence in sumatrol itself is clearly established by the formation of a crystalline O-*acetyldehydrosumatrol* having a negative ferric reaction.

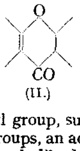
Hydrogenation of sumatrol was readily accomplished with the aid of a platinum catalyst and gave rise to approximately equal amounts of two optically active products, *dihydro-* and *tetrahydro-sumatrol*, which were readily separated by taking advantage of the fact that the latter derivative is easily soluble in 2% aqueous sodium hydroxide. Dehydrogenation of these compounds by the iodine method yielded *dehydrodihydro-* and *dehydrotetrahydro-sumatrol* respectively. Of these, only the former is optically active. Dehydrodihydrosumatrol was also obtained by the hydrogenation of dehydrosumatrol, but in this case the alkali-soluble fraction of the product, which in all probability consisted largely of dehydrotetrahydrosumatrol, could not be purified.

On being boiled with aqueous alcoholic potassium hydroxide, dehydrosumatrol was converted by the addition of the elements of two molecules of water into a monobasic acid, *sumatrolic acid*. Similarly, dehydrodihydrosumatrol furnished a product which, though it has not yet been obtained pure, is undoubtedly dihydrosumatrolic acid.

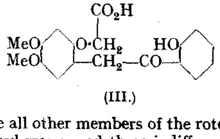
The isomerism of sumatrol with tephrosin and toxicarol, its insecticidal activity, and its co-existence with rotenone and toxicarol (or a toxicarol precursor) in the same plant, which we believe in the circumstances argues a close biogenetic relationship, clearly appear to justify the assumption that sumatrol is closely related structurally to other members of the rotenone series. Although we have not yet been able to complete our studies on the degradation of the compound, nevertheless, starting with this hypothesis, we are able to allocate rational structural formulæ to sumatrol and its derivatives.



(I.)



(II.)



(III.)

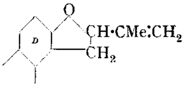
Apart from the phenolic hydroxyl group, sumatrol, like all other members of the rotenone series, possesses two methoxyl groups, an active carbonyl group, and three indifferent oxygen atoms. Further, sumatrol and dihydrosumatrol can be almost quantitatively dehydrogenated to give dehydro-derivatives which furnish acids of the derrisic acid type by standard procedures. It therefore appears practically certain that sumatrol possesses

the chromanochromanone residue (I) which gives the chromenochromone type (II) capable of forming the derrisic acid type (III) (J., 1933, 489, 1163; 1935, 993).

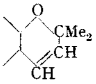
Since it has been clearly established that, like its isomeride toxicarol, sumatrol has a phenolic hydroxyl group in the *o*-position to the carbonyl group, this hydroxyl group must be at the 5-position of the chromanochromanone (I) (*i.e.*, ring *D*). Apart from the ferric reaction, the possibility that the hydroxyl group is at the 2- or 3-position is excluded, because, unlike tephrosin and the rotenolones-I and -II (Takei and co-workers, *Ber.*, 1933, **66**, 479), sumatrol and its hydrogenation products cannot be dehydrated and give dehydro-products by oxidation only. Since in all members of the rotenone series ring *D* carries two ethereal oxygen atoms, consequently in sumatrol this ring is either a hydroxyquinol or a phloroglucinol residue. Comparison of the ferric reactions of sumatrol and toxicarol and of their respective derivatives, as set out below, indicates that in sumatrol ring *D* of (I) is in all probability a phloroglucinol residue (compare J., 1935, 681).

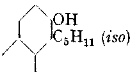
	Sumatrol.	Toxicarol.
Parent compound	Brown, tinged green.	Deep green.
Dehydro-compound	Deep green.	,, ,,
Dihydro-compound	Brown.	Brown.
Tetrahydro-compound	Olive-green.	—
Dehydrodihydro-compound	Deep green.	Deep green.
Dehydrotetrahydro-compound	,, ,,	—

All the known members of the rotenone series may be considered to be built up from the chromanochromanone type (I) by addition of an isoprene residue forming a fifth ring system fused to ring *D* which is of one of the following types—(IV), present in rotenone, (V) in *iso*rotenone, and (VI) in deguelin, tephrosin, and toxicarol.


(IV.)

(V.)


(VI.)

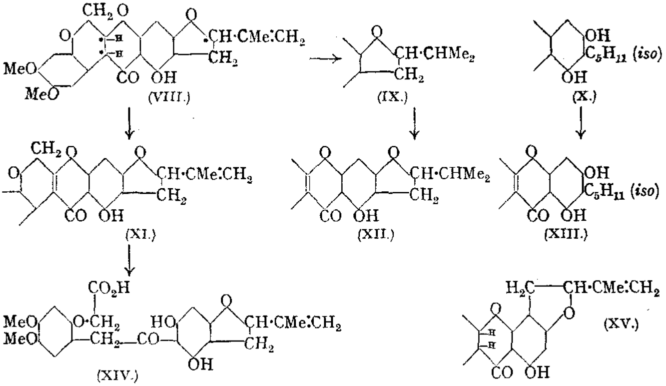

(VII.)

On hydrogenation, types (V) and (VI) behave normally, giving saturated dihydro-derivatives, but the *iso*propenyl type (IV) gives in addition to an *iso*propyldihydrofuran an alkali-soluble tetrahydro-product, *e.g.*, tetrahydrorotenone (or dihydrorotenonic acid of older nomenclature) type (VII). The behaviour of sumatrol in forming an alkali-insoluble saturated dihydro- and an alkali-soluble tetrahydro-derivative on hydrogenation is identical with that of rotenone and therefore we consider that the sumatrol molecule contains the system (IV). Consequently it would appear that sumatrol is a 5-hydroxyrotenone and may be represented by formula type (VIII) and hence dihydro-, tetrahydro-, dehydro-, dehydrodihydro- and dehydrotetrahydro-sumatrol have formula types (IX), (X), (XI), (XII) and (XIII) respectively.

The structure type (VIII) suggested for sumatrol possesses three asymmetric carbon atoms (marked*). In the formation of dihydrosumatrol (IX) none of these centres is affected, but in the conversion of both sumatrol and dihydrosumatrol into the respective dehydro-derivatives (XI) and (XII) the two centres at C_2 and C_3 in the chromanochromanone residue are destroyed and, since these compounds are both optically active, the asymmetric C-atom in the dihydrofuran system is a centre of optical activity. In the formation of tetrahydrosumatrol, which is optically active, the latter centre of activity is destroyed and therefore the C-atoms at positions 2 and 3 of the chromanochromanone residue are also centres of optical activity, a conclusion in agreement with the fact that the optically active centres C_2 and C_3 are destroyed in the dehydrogenation of tetrahydrosumatrol, thus giving an optically inactive dehydro-derivative.

The foregoing optical rotation phenomena observed for sumatrol and its hydrogenation and dehydrogenation products are identical with those exhibited by rotenone and its corresponding derivatives, thus affording strong evidence in support of the structural formulæ proposed for sumatrol and its degradation products. Further, these structures are also supported by the fact that the dehydro-compounds (XI) and (XII), like the members

of the dehydrorotenone series, are converted into acids of the derrisic acid type, of which that obtained from (XI) may be represented by formula type (XIV).



The formulæ (VIII), (IX), (XI) and (XII) proposed for sumatrol and its derivatives are of the linear type with respect to rings *C*, *D*, and *E*, but, as is obvious, the angular type (XV) present in rotenone may well obtain. The facts at our disposal do not permit us to make a choice between these two types, but the existence of a number of linear furanocoumarins (bergapten type) having a phloroglucinol nucleus (*iso*bergapten appears to be the only angular type known) might possibly be considered to favour the same structure for sumatrol.

By analogy with rotenone it should be possible according to formulæ (VIII) and (XI) to isomerise sumatrol and dehydrosumatrol by conversion of the *iso*propenyldihydrofuran system into an *iso*propylfuran residue, *i.e.*, conversion of (IV) into (V), and, although all attempts to effect this change have been unsuccessful (see experimental section), it should be emphasised that in no case was the starting material recovered unchanged (compare Cahn and Boam, *loc. cit.*).

Experimental.

Sumatrol.—The compound was isolated from the resin by the method described by Cahn and Boam (*loc. cit.*), but the yield (40 g.) of crude material separating from the carbon tetrachloride solution of the resin (500 g.) was increased somewhat by keeping this solution for 4 weeks. Repeated extraction of the crude product with boiling alcohol (first portion of 150 c.c.; succeeding portions, 50 c.c.) gave a series of twelve to thirteen fractions, having m. p. from 168—172° to 194—195°, of which the final fraction was almost pure sumatrol. Repeated crystallisation from alcohol (less wasteful than acetone) finally gave the compound in slender needles which, on being collected immediately and pressed on porous tile, had m. p. 192—194°. After having been kept in air for 2—3 days (on one occasion for only 6 hours), the dried material had m. p. 195—196°, $[\alpha]_D$ − 184° (*c*, 1·335 in benzene) [Found: C, 67·2, 67·2; H, 5·4, 5·4; OMe, 16·5; *M*, 396, 383. Calc. for $C_{21}H_{16}O_5(OMe)_2$: C, 67·3; H, 5·4; OMe, 15·1%; *M*, 410]. In view of the melting point phenomena of sumatrol observed by Cahn and Boam the following observations are recorded: Recrystallisation of the material, m. p. 195—196°, from acetone gave colourless needles, m. p. 194°, unaltered after the compound had been kept for several days. On one occasion pure sumatrol was twice recrystallised from acetone and each time had a constant m. p. of 194°, but on being recrystallised for a third time the compound had m. p. 183°, which after 3 days changed to 192—194° and then remained constant. A small specimen of sumatrol kindly presented to us by Dr. Cahn and labelled m. p. 189° was found to have m. p. 187—188° and after being recrystallised from alcohol and dried for 3 days had m. p. 194—195°.

Sumatrol is sparingly soluble in methyl alcohol, cold acetic acid, and in 8% aqueous sodium hydroxide, moderately soluble in ethyl acetate and benzene, and readily soluble in chloroform. With alcoholic ferric chloride it gives a deep brown coloration tinged with green, which is unaltered on dilution with water. A mixture of sumatrol (0·5 g.), hydroxylamine hydrochloride (0·5 g.), and dry pyridine (5 c.c.) was heated on the steam-bath for 20 hours, cooled, and poured on ice. After being kept for 1 hour, the resulting *oxime* was collected, washed, dried, and crystallised from alcohol and then from 50% alcohol, forming colourless slender needles, m. p. 245—247° (Found : C, 65·1, 65·1; H, 5·6, 5·6; N, 3·5. $C_{23}H_{23}O_7N$ requires C, 64·9; H, 5·5; N, 3·3%). When the reaction mixture was heated for shorter periods, oximation appeared to be incomplete and a mixed product resulted.

The following attempts to isomerise sumatrol proved unsuccessful: Sumatrol (0·5 g.), suspended in acetic acid (3·5 c.c.), was treated with concentrated sulphuric acid (1·5 c.c.), and the mixture kept at 60—65° for 12 minutes, gradually heated to 95° in the course of 10 minutes, and then maintained at this temperature for 8 minutes. The product obtained by addition of much ice to the reaction mixture separated from hot alcohol in tiny yellow spherical masses, which gave a deep green ferric reaction. Addition of methyl alcohol (3 vols.) to a warm solution of this product in hot chloroform (1 vol.) caused the separation of a similar solid, but all attempts to obtain crystalline material were unsuccessful. The products melted over a range which varied, according to the solvent used, from 190° to 210°. Amorphous material was also obtained when sumatrol (0·25 g.) was dissolved in concentrated sulphuric acid (4 c.c.) in the course of 4 minutes, and the product precipitated with ice-water. In another experiment a mixture of acetic acid (3 c.c.) and sulphuric acid (1 c.c.) containing sumatrol (0·5 g.) was gently refluxed for 2 minutes, cooled, and poured on ice; only a small amount of a dark amorphous solid separated from a cooled alcoholic solution of the product.

When a solution of sumatrol (0·5 g.) in alcohol (80 c.c.) containing concentrated sulphuric acid (8 g.) was refluxed for 4 hours, the crystalline material (0·4 g.) which separated from the cooled solution consisted of unchanged sumatrol, m. p. and mixed m. p. 195—196°.

Dehydrosumatrol.—Iodine (1·2 g.), dissolved in a little alcohol, was added in the course of 5—10 minutes to a solution of sumatrol (1 g.) in boiling alcohol (140 c.c.), containing sodium acetate (3 g.), and the mixture then boiled for 1¾ hours; after the addition of the greater part of the iodine (about 1 g.) the solution retained a permanent brown colour. Next day the resulting crystalline iodo-derivative (0·45 g.) was collected, washed, and dried; a further quantity (0·9 g.) of crude iodo-compound was obtained when the alcoholic filtrate was reduced to a volume of 20 c.c. and the residue treated with water (200 c.c.). The crystalline product gave a deep green ferric reaction and on being heated decomposed at about 200°.

A mixture of the iodo-derivative (0·45 g.), acetic acid (10 c.c.), and zinc dust (0·8 g.) was refluxed for 2 hours; after 1½ hours more zinc (0·4 g.) was added. The hot solution was filtered, and the zinc washed with boiling acetic acid (5 c.c.). On cooling, the combined solutions deposited the *dehydro*-compound (0·3 g.), which separated from chloroform–methyl alcohol in tiny, pale yellow prisms, $[\alpha]_D$ — 55° (*c*, 2·500 in chloroform), m. p. 190—192°, containing an indefinite amount of solvent of crystallisation [Found in material dried at 80° in a high vacuum : C, 67·4, 67·4, 67·6; H, 4·9, 4·9, 5·0; OMe, 15·1. $C_{21}H_{14}O_5(OMe)_2$ requires C, 67·6; H, 4·9; OMe, 15·2%]. This compound is readily soluble in chloroform, sparingly soluble in hot methyl alcohol, and slightly soluble in warm benzene, acetone, or ethyl acetate. With alcoholic ferric chloride it gives a deep green coloration.

Acetylation of dehydrosumatrol (0·35 g.) with acetic anhydride (5 c.c.) and pyridine (2·5 c.c.) at 100° for 1 hour and then at room temperature for 18 hours gave rise to the *acetate* (0·38 g.), which separated from chloroform–methyl alcohol in clusters of pale yellow needles, m. p. 256—259° after darkening at 250°, having a negative ferric reaction [Found: C, 66·3; H, 5·0; CH_3·CO, 11·7. $C_{23}H_{19}O_7(CH_3·CO)$ requires C, 66·7; H, 4·9; CH_3·CO, 9·6%].

Attempts to isomerise dehydrosumatrol (0·3 g.) with warm acetic acid (5 c.c.) and sulphuric acid (1·7 c.c.) gave rise to a product which separated as an amorphous solid, m. p. 170—178°, from chloroform–methyl alcohol and gave a deep green ferric reaction.

Hydrogenation of Sumatrol.—Absorption of hydrogen (approx. 1·5 mols.) by sumatrol (1 g.), dissolved in ethyl acetate (200 c.c.) containing a platinum catalyst (0·15 g., prepared according to directions of Adams, Voorhees and Shriner, " Org. Synth.," Coll. Vol. I, 1932, p. 452), ceased in about 45 minutes. After the removal of the catalyst, the volume of the solution was reduced to 75 c.c., an equal volume of ether added, and the mixture extracted several times with 2% aqueous sodium hydroxide. Acidification of the combined extracts with dilute hydrochloric acid gave *tetrahydrosumatrol* (0·5 g.), which separated from chloroform–methyl alcohol in colourless, stout,

well-formed prisms, m. p. 222—223°, containing solvent of crystallisation, $[\alpha]_D$ + 122° in chloroform (*c*, 1·0827) [Found in material dried in a high vacuum at 100° : C, 66·7, 66·7; H, 6·3, 6·3; OMe, 14·9, 14·6. $C_{21}H_{20}O_5(OMe)_2$ requires C, 66·6; H, 6·3; OMe, 15·0%]. This compound is more soluble in alcohol than the parent compound. Addition of one drop of ferric chloride to an alcoholic solution of tetrahydrosumatrol gives an almost black coloration, which becomes violet-brown on addition of water. With more ferric chloride the black solution becomes olive-green.

The ether–ethyl acetate solution left on removal of the tetrahydro-derivative was washed with water, dried, and evaporated. Crystallisation of the residue (0·45 g.) from chloroform–methyl alcohol gave *dihydrosumatrol* in colourless slender rods, m. p. 184—185°, $[\alpha]_D$ − 32° (*c*, 0·2667 in chloroform) [Found: C, 66·8, 66·8; H, 6·0, 6·0; OMe, 15·6. $C_{21}H_{18}O_5(OMe)_2$ requires C, 67·0; H, 5·9; OMe, 15·1%], which gave a deep brown coloration with alcoholic ferric chloride, unchanged on addition of water.

Dehydrodihydrosumatrol.—Iodine (0·7 g.) was added to a solution of dihydrosumatrol (0·7 g.) in boiling alcohol (70 c.c.) containing sodium acetate (1·8 g.) in the course of 5 minutes, and the mixture refluxed for 1¾ hours. 20 Minutes later, pale yellow crystals of the iodo-compound began to separate and next day this product (0·26 g.), m. p. 191°, was collected; a further quantity of crude material (0·7 g.) was obtained by concentration of the alcoholic liquors and the subsequent addition of water. Acetic acid (13 c.c.), containing the iodo-compound (0·4 g.) and zinc dust (0·8 g.), was refluxed for 1½ hours; after ¾ hour, more zinc (0·4 g.) was added. After the removal of the zinc (wash with 5 c.c. of boiling acetic acid) the cooled solution deposited *dehydrodihydrosumatrol* (0·25 g.), which crystallised from chloroform–methyl alcohol and then chloroform–acetone as a matte of slender yellow needles, m. p. 235°, $[\alpha]_D$ − 63° (*c*, 0·2700 in chloroform), sparingly soluble in hot alcohol or acetone, readily soluble in hot benzene, and giving a deep green coloration with alcoholic ferric chloride (Found: C, 67·5, 67·4; H, 5·6, 5·5. $C_{23}H_{22}O_7$ requires C, 67·3; H, 5·4%). The yield of the dehydro-compound was approx. 70% of the theoretical.

Dehydrotetrahydrosumatrol.—A solution of iodine (2·3 g.) in alcohol (25 c.c.) was gradually added to a boiling solution of tetrahydrosumatrol (2·2 g.) in the same solvent (150 c.c.), containing sodium acetate (6·5 g.), the mixture refluxed for 1¾ hours, the greater part of the alcohol distilled, and the residual liquid (25 c.c.) mixed with water (200 c.c.). 3 Hours later, the solid (2·4 g.) was collected, washed, dried, and heated with boiling acetic acid (30 c.c.) and zinc dust (5 g., added in two portions of 4 g. and 1 g.) for 1½ hours. After removal of the zinc dust by filtration (wash with 5 c.c. of hot acetic acid) the combined solution and washings were diluted with water (200 c.c.). Repeated crystallisation of the product (2 g.) from alcohol (charcoal) gave *dehydrotetrahydrosumatrol* in pale yellow plates (1·1 g.), m. p. 218°, giving a deep green coloration with alcoholic ferric chloride and showing a zero rotation (Found in material dried in a high vacuum at 100° : C, 67·0, 67·2; H, 5·9, 6·0. $C_{23}H_{24}O_7$ requires C, 67·0; H, 5·9%).

Acetylation of this compound (0·14 g.) with acetic anhydride (2 c.c.) and pyridine (1 c.c.) at 100° for 1 hour and then at room temperature for 48 hours gave the *diacetate*, which separated from aqueous acetone in tiny, pale straw-coloured needles, m. p. 197°, having a negative ferric reaction and insoluble in 8% aqueous sodium hydroxide (Found: C, 65·5; H, 5·7. $C_{27}H_{28}O_9$ requires C, 65·3; H, 5·7%).

Sumatrolic Acid.—A mixture of dehydrosumatrol (0·7 g.), potassium hydroxide (3·5 g.), zinc dust (0·7 g.), alcohol (65 c.c.), and water (5 c.c.) was refluxed for 6 hours, filtered, and diluted with water (65 c.c.), the greater part of the alcohol was removed by distillation, and the cooled residue was acidified with hydrochloric acid. 24 Hours later, the semi-solid was collected, washed, and dissolved in aqueous sodium bicarbonate. After having been filtered to remove traces of insoluble material, the solution was acidified with hydrochloric acid, the pale pink solid (0·5 g.) thus precipitated was dried and dissolved in a little hot acetone, and the solution was treated with charcoal, filtered, diluted with benzene (3 vols.), and then evaporated until crystalline material began to separate. Purification of the product which separated from the cooled liquor was repeated several times from hot benzene containing a little chloroform, finally giving *sumatrolic acid* in spherical aggregates of rather ill-defined colourless crystals, m. p. 150°, readily soluble in alcohol, chloroform, acetone, or ethyl acetate and sparingly soluble in hot benzene or water (Found: C, 62·2; H, 5·9. $C_{23}H_{24}O_9$ requires C, 62·1; H, 5·5%). With alcoholic ferric chloride this acid gives a violet coloration.

Hydrolysis of dehydrodihydrosumatrol (0·3 g.) with boiling aqueous-alcoholic potassium hydroxide (1·6 g. of hydroxide in 5 c.c. of water and 30 c.c. of alcohol) in the presence of zinc dust (0·4 g.) for 3½ hours and purification of the crude product with aqueous sodium bicarbonate gave rise to a solid which separated from benzene in short rods, m. p. 130—132°; this un-

doubtedly consisted of almost pure dihydrosumatrolic acid, but was not obtained analytically pure owing to lack of material.

Hydrogenation of Dehydrosumatrol.—Dehydrosumatrol (1 g.), dissolved in ethyl acetate (400 c.c.), was treated with a platinum oxide catalyst (0·15 g.) and hydrogen; absorption (approx. 1·5 mols.) was complete in about 20 minutes. After the removal of the catalyst the solvent was evaporated, leaving a bright yellow solid, which, by means of 2% aqueous sodium hydroxide, was resolved into an alkali-soluble and an alkali-insoluble fraction. After being extracted three times with boiling acetone (5 c.c.) to remove traces of impurities, the latter consisted of dehydrodihydrosumatrol, m. p. 235°, unaltered by recrystallisation from chloroform–acetone, and was identified by comparison with an authentic specimen, m. p. and mixed m. p. 235°. The alkali-soluble fraction separated readily from warm alcohol in pale yellow crystals, which, however, could not be obtained homogeneous but appeared to consist mainly of dehydrotetrahydrosumatrol.

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UNIVERSITY OF LIVERPOOL. [*Received, February 18th*, 1937.

112. *Electrolytic Dissociation Processes. Part II. The Friedel–Crafts Reaction.*

By FRED FAIRBROTHER.

A TRANSITION from a covalent binding to an ionic binding can be brought about in several ways. In Part I (J., 1936, 847) it was shown that, on the dissolution of iodine monochloride in carbon tetrachloride or *cyclo*hexane, an augmentation of the dipole moment occurred, and that, as the polarisability of the solvent was increased, the solutions gradually became conducting. A similar augmentation of the dipole moment under the influence of solvation was shown in the case of the hydrogen halides (Fairbrother, J., 1932, 43; 1933, 1541; *Trans. Faraday Soc.*, 1934, **30**, 862).

In addition to the action of solvation in bringing about such a transition, it is to be expected that a similar effect will be produced by the proximity to the dipole in question, of molecules which possess the power of forming complexes with the outer end of the dipole. In the case of simple solvation we may be dealing chiefly with coulombic forces between the ions and the solvent molecules; these lead to ionisation (as distinct from electrolytic dissociation, which it precedes) only of such molecules in which the potential energies of the covalent and ionic states are not widely separated. In the case of complex formation we have also the formation of a chemical bond between one of the potential ions and a part of its environment, resulting effectively in the formation of an ion of larger radius and the same charge, which is consequently less tightly bound to its fellow. Thus, Lowry (*Chem. and Ind.*, 1923, **42**, 1048) and Brønsted (*Rec. trav. chim.*, 1923, **42**, 718) have pointed out that a hydracid only gives rise to hydrogen ions in the presence of molecules (*e.g.*, water) which can combine with the proton, and Lowry (*Phil. Mag.*, 1923, **46**, 964) has discussed at length the process of "intramolecular ionisation" as a precursor to many organic reactions. Also, Meerwein (*Annalen*, 1927, **455**, 227) has shown that many weak electrolytes are increased in strength by the formation of complex ions.

A transition of a covalent carbon–chlorine bond into an ionic bond, through complex formation, appears to occur as the first step in the well-known Friedel–Crafts synthesis. This reaction, of which there are many forms, has been studied in the present work in its application to the synthesis of acetophenone from benzene and acetyl chloride and of β-phenyl-β-methylpropane from benzene and *tert.*-butyl chloride.

Friedel and Crafts expressed the opinion (*Compt. rend.*, 1877, **85**, 74) that the first step in the reaction was the formation of a double compound between the benzene and the aluminium chloride, with the elimination of hydrogen chloride, $C_6H_6 + Al_2Cl_6 = C_6H_5{\cdot}Al_2Cl_5 + HCl$, and the subsequent reaction of the double compound with the aliphatic chloride and the regeneration of the aluminium chloride. They explained the apparent

absence of reaction between the aluminium chloride and the benzene on the assumption that the double compound was unstable and was formed only in small quantities at a time. The view that some kind of double compound is formed between the aluminium chloride and one or other or both of the reactants as the first step in the reaction, has been generally held for a long time, and Perrier (*Compt. rend.*, 1893, **116**, 1298; *Ber.*, 1900, **33**, 815) and Böeseken (*Rec. trav. chim.*, 1900, **19**, 19; 1901, **20**, 102) isolated crystalline compounds of aluminium chloride with acid chlorides. But the fact that some Friedel–Crafts reactions could be carried out with much less than the molecular proportion of aluminium chloride led Böeseken (*ibid.*, 1904, **23**, 1904) to suggest that the intermediate-compound theory should be replaced by a catalytic hypothesis according to which the molecules were activated by the catalyst, combination then occurring between these activated molecules with the subsequent evolution of hydrogen chloride. Later (*ibid.*, 1910, **29**, 85), he suggested that the action of the aluminium chloride was due to a "dislocating influence" on the molecules, this influence being exerted where the molecules were weakest: "in organic chlorides it is probably the chlorine atom which is thus activated."

A new aspect has been given to the intermediate-compound hypothesis by Meerwein (*Annalen*, 1927, **455**, 227) and Hückel ("Theoretische Grundlagen der Organischen Chemie," 1931, Vol. 1, p. 351), who regard the complexes which are formed as co-ordination compounds containing the complex anion $[AlCl_4]^-$, thus: $CH_3{\cdot}COCl + AlCl_3 \longrightarrow (CH_3{\cdot}CO)^+ + [AlCl_4]^-$. Such a process would constitute effectively a conversion of the covalent carbon–chlorine bond into an ionic bond.

The ability of aluminium chloride to form complexes was explained by Lewis ("Valence and the Structure of Atoms and Molecules," New York, 1923, p. 99) on the basis that "aluminium, like boron, frequently completes its group of 8 (electrons) by attaching to itself a lone pair belonging to another atom." Thus, it forms the stable compound $AlCl_4K$, which would presumably have the anion $[AlCl_4]^-$ in the fused state (Hildebrand, "Solubility," New York, 1936, p. 115).

There are, therefore, three main possibilities in the Friedel–Crafts mechanism: (1) the formation of an intermediate compound between the benzene and the aluminium chloride, as suggested by Friedel and Crafts, (2) a physical catalysis wherein the molecules of the reactants are "activated," (3) the formation of a co-ordination compound between the aliphatic chloride and the aluminium chloride, in which the organic chlorine atoms leave the carbon atoms completely and enter a complex anion $[AlCl_4]^-$ which is able to rotate relatively to the carbonium ion prior to the evolution of hydrogen chloride. [The formation of a complex molecule, *e.g.*, $R{\cdot}COCl,AlCl_3$, in which each aluminium atom is found at the end of the reaction to be combined with the same chlorine atoms with which it started, is hardly to be differentiated from (2).]

The use of aluminium chloride in which part of the chlorine atoms are unstable isotopes, *i.e.*, radioactive, offers a means of deciding between these possibilities. If the mechanism were as (1), the evolved hydrogen chloride would be more radioactive than an equivalent amount of the final reaction mixture, since the organic chloride would act as a diluent of the latter: if it were as (2), then the hydrogen chloride when first formed would be wholly inactive. If the mechanism were as (3), then, since all the chlorine atoms concerned in the reaction would have an equal chance of escaping as hydrogen chloride, a complete interchange between the active and inactive chlorine atoms would take place. A complete interchange of this character has now been found experimentally.

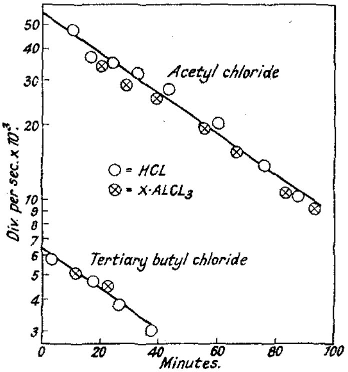
This, however, does not, by itself, entirely eliminate the possibility that the interchange of chlorine atoms may have taken place, subsequent to the actual reaction, between the hydrogen chloride and the catalyst, though complex formation does not appear to take place readily between the hydrogen chloride and the aluminium chloride, and every hydrogen chloride molecule would have to form an $AlCl_4H$ complex and be re-evolved as hydrogen chloride for equality of interchange by such a process. Also, there is some indication that, in the Friedel–Crafts synthesis of ketones, the combined aluminium chloride is not immediately liberated but remains as part of a double compound with the ketone, and interchange with the uncombined aluminium chloride could only occur as a heterogeneous reaction.

It has also been shown experimentally by the use of radioactive aluminium chloride, however, that an interchange of chlorine atoms takes place between acetyl chloride and aluminium chloride, $CH_3{\cdot}COCl + AlCl_3 \longrightarrow (CH_3{\cdot}CO)^+ + [AlCl_4]^-$, in the absence of any third reactant or evolution of hydrogen chloride.

Experimental.

Materials.—Merck's thiophen-free benzene was dried over phosphoric oxide and distilled. Acetyl chloride of C.P. quality was fractionated before use. *tert.*-Butyl chloride (Eastman Kodak) was dried over phosphoric oxide and distilled. The aluminium chloride was taken from a new bottle of " Reagent " quality.

Procedure.—About 0·5 g. of coarsely powdered aluminium chloride was placed in a shallow aluminium tray, covered with thin aluminium foil, and exposed to a beam of deuterons of about 5 million volts energy, produced by the Cyclotron described by Lawrence and Cooksey (*Physical Rev.*, **1936**, **50**, 1131), for about 30 microampère-minutes. The irradiation was carried out in air, and the target was water-cooled to avoid volatilisation of the aluminium chloride. The active sample was then mixed with excess of inactive aluminium chloride (about 10 g. in all), quickly ground to a fine powder, and placed in a 200-c.c. flask attached to a ground-in reflux condenser and dropping funnel. The aluminium chloride was immediately covered with 8 c.c. of dry benzene, and 6—7 g. of acetyl chloride were slowly added from the dropping-funnel, the residue in the funnel being washed into the reaction mixture with a further 5 c.c. of dry benzene. The evolved hydrogen chloride was passed through a 10-cm. plug of glass-wool to catch any spray, and absorbed by 5*N*-potassium hydroxide. When apparent reaction had ceased, the mixture was gently boiled under reflux for 15 minutes, and the hydrogen chloride in the flask blown out by a gentle stream of air dried by phosphoric oxide. The residue in the flask was poured slowly into cold water, a little nitric acid added, and the organic matter extracted with ether. The chloride in the aqueous portion was precipitated with silver nitrate, and the silver chloride washed and dried. The potassium chloride produced in the absorption of the hydrogen chloride was also converted into dry silver chloride. Equal weights of the two samples of silver chloride were then dissolved in equal volumes of concentrated aqueous ammonia, and placed in thin glass test-tubes (1 cm. diam.) which could be introduced directly in a fixed position inside the case of a sensitive quartz-fibre electroscope. The glass tubes were lightly coated on the outside with " Aqua-dag " graphite to form a conducting layer and prevent electrostatic disturbance of the electroscope needle. Readings were then taken alternately of the activities of the two samples of chloride. The use of an ammoniacal solution of the silver chloride, instead of the solid, permits, as shown by Olson, Libby, Long, and Halford (*J. Amer. Chem. Soc.*, **1936**, **58**, 1313), a better reproducibility of the geometry of the system. The total time taken from the removal of the sample from the Cyclotron to the commencement of readings was slightly under 2 hours, or about 3 half-lives of the radio-chlorine. In the process of activation a radioactive isotope of aluminium $^{28}_{13}Al$ would also be obtained (Lawrence, *Physical Rev.*, **1934**, **46**, 746), but as this has a half-life of only 153 secs. it would not interfere with the measurements, and in any case, most of it would be removed in the precipitation with silver nitrate.



The results are shown in the figure, in which the movement of the quartz fibre, in divisions per sec. $\times 10^3$ (minus the background drift), is plotted logarithmically against the time of observation. The results for the two samples of silver chloride—from the hydrogen chloride and from the reaction residue, $X{\cdot}AlCl_3$—are suitably differentiated. The lines drawn across the diagram correspond to a half-life of 37 minutes (Olson *et al.*, *loc. cit.*). The activities of the

two samples of silver chloride do not differ by more than about 10%, which is probably due to accumulated experimental errors, and the interchange may therefore be regarded as complete. A similar result was obtained with *tert.*-butyl chloride and benzene except that, the sample of aluminium chloride not being so active as in the first case, it was not possible to follow the decay curves for so long.

In order to show that the interchange can take place between acetyl chloride itself and the aluminium chloride, 5 g. of a similar mixture of active and inactive aluminium chloride were placed in a glass tube attached to a vacuum distillation apparatus, and 3 g. of acetyl chloride were added slowly with cooling. The mixture was kept for a few minutes at room temperature, and then the pressure was reduced : very little acetyl chloride (condensed in liquid air) distilled over at a pressure of about 10^{-4} mm.; the mixture was then heated externally with water to about 50°, and a little more distilled at the same pressure. The distillate was examined directly, since the amount was insufficient for a quantitative treatment by the above procedure, and was found to possess a strong radioactivity, decaying with the half-life of 37 minutes characteristic of radio-chlorine. The distillation was carried out through a 10-cm. plug of tightly packed glass-wool to catch any spray.

It is therefore to be concluded that the first stage in the Friedel-Crafts reaction, for the synthesis of ketones or hydrocarbons, is the " ionisation " under the influence of the aluminium chloride, of the covalent aliphatic carbon-chlorine bond, with the formation of the ion $[AlCl_4]^-$ and a positive carbonium ion. Such a process constitutes, in a sense, " activation " of the aliphatic chloride, in that the ion pair in question is more reactive than the un-ionised chloride, and unless a stable complex is formed between the aluminium chloride and the final product, a small amount of aluminium chloride will serve to " activate " a large amount of organic chloride. The Friedel-Crafts synthesis includes a variety of reactions and the use of several different metallic chlorides as catalysts : whether the above considerations apply quite generally is a matter for further investigation.

I wish to thank the Leverhulme Trustees for the grant of a Fellowship, and Prof. Ernest O. Lawrence for the facilities necessary for this work.

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113. *The Interactions of Cobalt Chloride and Ethylenediamine.*

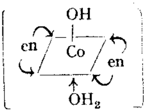
By H. D. K. DREW and N. H. PRATT.

AN aqueous solution containing cobalt chloride and ethylenediamine in molecular proportion, when kept in a limited supply of air, deposited minute pink crystals containing both cobaltic and cobaltous cobalt; the mother-liquor, on slow evaporation, yielded the purplish *cis*-compound (I), and other products. The pink substance proved to be trans-*hydroxoaquobisethylenediaminocobaltic cobaltochloride* (II), which appears to be the only known example of this type. The structure of (II) was determined by conversion into the brownish-pink trans-*plato-salt* (III) by means of potassium chloroplatinite, and then, by double decomposition with tetramminoplatinous chloride, into the reddish *trans*-chloride (IV), together with the insoluble green salt of Magnus. The chloride (IV) was recognised as the *trans*-compound by its properties (Werner, *Ber.*, 1907, **40**, 272); and reconversion of (IV) into (III) showed, as would be anticipated, that change of configuration had not taken place.

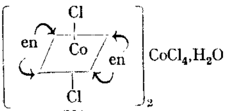
The action of dilute hydrochloric acid on (II) gave dark green trans-*dichlorobisethylenediaminocobaltic cobaltochloride monohydrate* (V), which with potassium chloroplatinite gave the green *trans*-plato-salt (VI) of Jörgensen (*J. pr. chem.*, 1890, **41**, 440). With less dilute hydrochloric acid, (II) gave bluish-green trans-*trichloroethylenediaminocobaltiethylenediamine hydrochloride*, (VII), a dihydrated form of which has been described by Jörgensen (*ibid.*, 1889, **39**, 24), although we have not been able to obtain it; (VII) readily lost hydrogen chloride to give Jörgensen's light green *trans*-salt (VIII), which with potassium chloroplatinite yielded (VI) (see Werner, *Ber.*, 1901, **34**, 1705). It follows that both (V) and (VII) belong to the *trans*-(praseo)series and that the action of hydrochloric acid on

(II) is configuratively normal. It is evident also that the hydrochloride (VII), for which a structural formula has not hitherto been proposed, must be constituted as shown, with

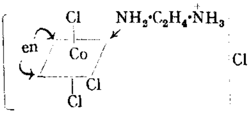
$[CoCl_2en_2]Cl$ (I.) $[Co(H_2O)(OH)en_2]PtCl_4$ (III.) $[Co(H_2O)(OH)en_2]Cl_2$ (IV.)



(II.)



(V.)



(VII.)

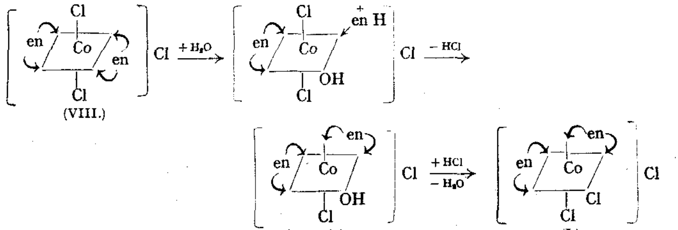
$[CoCl_2en_2]_2PtCl_4$ (VI.) $[CoCl_2en_2]Cl$ (VIII.) $[CoCl(NH_3)en_2]Cl_2$ (IX.)

the free positive charge located upon an opened ethylenediamino-loop of (VIII). This is in agreement with the results previously obtained in the opening of chelate loops attached to platinum (Drew and Tress, J., 1932, **2328**; 1933, **1335**).

The reconversion of (V) into (II) was effected by treatment with a very little alkali, and that of (VIII) into (II) by the same means in presence of aqueous cobalt chloride. *The removal of chlorine by alkali in the above reactions is thus again configuratively* normal.

The configuration of (V) was further confirmed by transforming it, by means of nitric acid, into the green *trans*-nitrate, $[CoCl_2en_2]NO_3$, identical with that obtained from (VIII) (Jörgensen, *J. pr. Chem.*, 1889, **39**, 23). When (V) was treated with a small excess of ammonia, however, it gave the *cis*-chloride (IX), which is red and forms a red plato-salt; this substance was recognised as the *cis*-form by transformation into the dithionate, $[CoCl(NH_3)en_2]S_2O_6$ (Werner, *Annalen*, 1912, **386**, 165). The action of ammonia upon (V) is therefore configuratively abnormal, as is the case also with (VIII) (Werner, *loc. cit.*, p. 58).

Jörgensen's remarkable transformation (*J. pr. Chem.*, 1889, **39**, 16) of the praseo (*trans*)-chloride (VIII) into the violeo (*cis*)-isomeride (I), by evaporation with water at 100°, was confirmed; the change is never quite complete, and moreover, it is not effected by slow evaporation at laboratory temperature. No explanation of the change has yet been given; the following scheme is suggested by the present experiments:

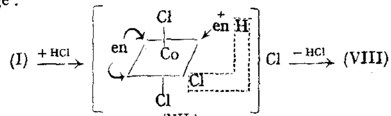


(VIII.) (racemic) (I.)

It will be seen that the elimination of hydrogen chloride could involve either of two similarly situated chlorine atoms in the kation of the second formula, giving enantiomorphous products, the final product (I) being therefore racemic.

The reverse transformation of the violeo- into the praseo-chloride (Jörgensen, *ibid.*, 1890, **41**, 449) by evaporation with dilute hydrochloric acid was likewise confirmed. The plato-salts (green and purple, respectively) of the two chlorides were shown to be isomeric.

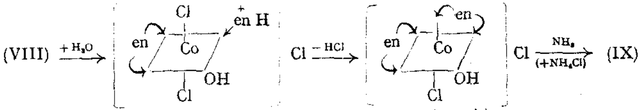
Here the formation of the hydrochloride (VII), which is known to condense to (VIII), explains the change :



(VII.)

In the case of either of the enantiomorphous *cis*-chlorides, (I), the chelate loop must open at a nitrogen atom in the *cis*-position with respect to both nitrogens of the unopened loop.

In accord with the foregoing, the following scheme explains why the replacement of halogen by ammonia, through the action of aqueous ammonia upon (VIII), or upon (V), is configuratively abnormal :



(racemic)

The last stage represents a displacement of hydroxyl by ammonia.

In other cases in which ammonia is known to bring about a change of configuration in a cobaltic salt, the application of this mechanism leads to the observed result without ambiguity at any stage, as may be seen in the following :

trans-$[CoCl(NH_3)en_2]Cl_2 \longrightarrow$ *cis*-$[Co(NH_3)_2en_2]Cl_3$;

cis-$[Co(NO_3)(NH_3)en_2](NO_3)_2 \longrightarrow$ *trans*-$[Co(NH_3)_2en_2](NO_3)_3$.

Where, as in the case of *cis*- or *trans*-$[CoCl(SCN)en_2]Cl$, the configuration of the product depends upon the experimental conditions, a second mechanism (probably that of direct replacement of halogen by ammonia) may be assumed to accompany the suggested mode of reaction.

Kurnakow (*Z. anorg. Chem.*, 1898, **17**, 223) combined cobalt chloride with the yellowish-brown salt $[Co\,en_3]Cl_3,3H_2O$ by evaporating an aqueous solution at 100°, and obtained dark green needles of the dihydrate (X). In our hands, his procedure invariably gave yellowish-green needles of the trihydrate (or, less probably, the tetrahydrate) (XI), which had the properties of a compound formulated by Werner (*ibid.*, 1900, **22**, 155) as $[Co\,en_3Cl_3]_2CoCl_2,4H_2O$; on one occasion only we obtained Kurnakow's compound by acidifying the solution with hydrochloric acid. These substances (X) and (XI), which are at once decomposed by water, are evidently assemblages of ions; their structures may be expressed, respectively, as (X*a*) (compare the case of Cs_3CoCl_5 ; Powell and Wells, J., 1935, 359) and (XI*a*). The blue ethylenediammonium salt of Kurnakow (*loc. cit.*, p. 215), of composition $CoCl_2,en_2,4HCl$, likewise unstable to water, probably has the structure $[en\,H_2]_2CoCl_6$, as written by Meyer and Hoehne (*Z. anorg. Chem.*, 1935, **222**, 163). On treating it with cobalt chloride in boiling hydrochloric acid, we obtained light blue crystals of an *octachloride* of composition $(en\,2HCl)_3CoCl_2$, which might be formulated as (XII) but for the lack of independent evidence of a co-ordination number of 8 for cobalt (compare Clément and Duval, *Compt. rend.*, 1935, **200**, 399). We have not been able to repeat the preparation of (XII). In several preparations of this series, very slight variations in the conditions lead to failure.

$CoCl_3\,en_3,CoCl_2,2H_2O$ (X.)

$2CoCl_3\,en_3,CoCl_2,3H_2O$ (XI.)

$[en\,H_2]_3CoCl_8$ (XII.)

$[Co\,en_3]\genfrac{}{}{0pt}{}{CoCl_4}{Cl}$ (X*a*.)

$[Co\,en_3]_2\genfrac{}{}{0pt}{}{CoCl_6}{Cl_2}$ or $[Co\,en_3]_2\genfrac{}{}{0pt}{}{CoCl_4}{Cl_4}$ (XI*a*.)

Experimental.

trans-*Hydroxoaquobisethylenediaminocobaltic cobaltochloride* (II) was prepared by gradually adding ethylenediamine (5 g.) to an ice-cold solution of hydrated cobalt chloride (19·8 g.) in water (50 c.c.), with constant stirring. The red-brown solution was left (1—2 days) in a stoppered vessel. The pink precipitate (1·5—2 g.) was filtered off (filtrate A), washed with water, alcohol, and ether, and dried over calcium chloride (Found: C, 11·7, 11·8; H, 5·2, 5·1; N, 13·6; Co, 28·2, 28·4. $C_4H_{19}O_2N_4Cl_4Co_2$ requires C, 11·6; H, 4·6; N, 13·5; Co, 28·4%). The substance formed minute transparent red rods, sparingly soluble in cold water but readily soluble in hot, and insoluble in alcohol. It was slowly decomposed by boiling water. The water molecule was not lost at 120°, but at 150° decomposition set in. Hydrogen peroxide oxidised the compound in the cold. It formed a brownish-pink trans-*plato-salt* (III) (Found: C, 8·6, 8·9; H, 3·8, 4·1; N, 10·4, 10·5. $C_4H_{19}O_2N_4Cl_4CoPt$ requires C, 8·7; H, 3·45; N, 10·2%). The plato-salt, ground with an equivalent aqueous solution of $[Pt(NH_3)_4]Cl_2$, gave Magnus's salt, which was filtered off, and a deep red solution which, on being allowed to evaporate, yielded red leaf-like crystals, with a bluish tinge, of the chloride (IV) (Found: C, 17·1; H, 6·6; N, 19·8; Co, 21·0. Calc.: C, 16·8; H, 6·7; N, 19·2; Co, 20·7%).

trans-*Dichlorobisethylenediaminocobaltic cobaltochloride monohydrate* (V) was prepared: (1) by treating the filtrate A (foregoing preparation) with an equal volume of concentrated hydrochloric acid, and evaporating the deep red liquid to about one-third of its volume; the resulting bluish-green liquid deposited dark green spangles, which were washed with concentrated hydrochloric acid, alcohol, and ether, and dried over phosphoric oxide; the compound may be recrystallised from 16% hydrochloric acid; (2) by evaporating a solution of (II) in 16% hydrochloric acid to crystallisation. The compound (Found: C, 13·3, 13·5; H, 5·1, 5·1; N, 15·4, 15·7; Co, 24·5, 24·6. $C_8H_{34}ON_8Cl_8Co_3$ requires C, 13·3; H, 4·7; N, 15·6; Co, 24·6%) was very soluble in water to a green neutral solution, becoming violet and then red on boiling; it was insoluble in alcohol. Addition of a little concentrated nitric acid to the aqueous solution precipitated light green crystals of the corresponding nitrate (Found: C, 15·55, 15·2; H, 5·6, 5·2; N, 22·6; Co, 18·9, 18·8. Calc.: C, 15·4; H, 5·1; N, 22·4; Co, 18·9%), the aqueous solution of which gave no precipitate with silver nitrate unless first boiled (whereupon it became red). Compound (V) formed the plato-salt (VI), dark green prisms (Found: C, 11·5, 11·7; H, 4·0, 3·9; N, 13·4. Calc.: C, 11·5; H, 3·8; N, 13·4%), which was also obtained from the above nitrate (Found: C, 11·6; H, 4·1; N, 13·4%). When the plato-salt was warmed with concentrated hydrochloric acid, it decomposed, giving yellow prisms of ethylenediammonium chloroplatinate, (en H_2)$PtCl_6$ (Found: C, 5·3; H, 2·4; N, 6·0; Pt, 41·2. Calc.: C, 5·1; H, 2·5; N, 5·9; Pt, 41·3%), described by Schacht (*Arch. Pharm.*, 1897, **235**, 459).

trans-*Trichloroethylenediaminocobaltiethylenediamine hydrochloride* (VII) was prepared by allowing the deep bluish-green solution of (II), or of (V), in concentrated hydrochloric acid to stand (1 or 2 days); the green rhombic plates which separated were washed with concentrated hydrochloric acid and dried over sulphuric acid (Found: C, 14·7; H, 5·5; N, 17·2; Co, 18·1. $C_4H_{17}N_4Cl_4Co$ requires C, 14·9; H, 5·3; N, 17·4; Co, 18·3%). The compound lost hydrogen chloride readily in air; its green solution in water was strongly acid. Attempts to repeat Jörgensen's method of preparation (*J. pr. Chem.*, 1889, **39**, 24) gave only ethylenediamine dihydrochloride and bisethylenediammonium cobalt chloride. When (VII) was powdered and heated at 100° (2 hours), it gave the *trans*-chloride (VIII); this formed green prisms from water (Found: C, 16·8; H, 5·9; N, 19·9; Co, 20·6. Calc.: C, 16·7; H, 5·6; N, 19·65; Co, 20·7%), and afforded the green plato-salt (VI) (Found: C, 11·6; H, 4·2; N, 13·7. Calc.: C, 11·5; H, 3·8; N, 13·4%). Aqueous solutions of (V) or (VIII), treated with ammonia until the green colour just became red, and then concentrated, gave red crystals of *cis*-chloroamminobisethylenediaminocobaltic chloride (IX) (Found: C, 15·8; H, 6·6; N, 22·9; Cl, 34·9; Co, 19·5. Calc.: C, 15·9; H, 6·3; N, 23·1; Cl, 35·2; Co, 19·5%); conversion of this into the dithionate by means of sodium dithionate yielded compact red prisms, distinct from the long needles of the *trans*-isomeride; the plato-salt of (IX) formed red cubes (Found: N, 12·5. Calc.: N, 12·3%).

Conversion of trans-*Dichlorobisethylenediaminocobaltic Chloride into its* cis-*Isomeride.*—The aqueous solution of the *trans*-chloride, evaporated to dryness on a water-bath, gave the *cis*-chloride (I), mixed with a little of the unchanged material. Repeated redissolution in water and evaporation failed to remove it, showing that the change is never completed. However, washing on a filter with a little water readily removed the more soluble praseo-salt. After being washed with water and alcohol and dried over phosphoric oxide, the violeo-salt appeared

to retain $\frac{1}{2}H_2O$ (Found: C, 16·2; H, 6·3; N, 19·2; Cl, 35·8; Co, 20·0, 20·1. Calc. for $C_4H_{16}N_4Cl_3Co,\frac{1}{2}H_2O$: C, 16·3; H, 5·8; N, 19·0; Cl, 36·2; Co, 20·0%). Evaporation of the violeo-chloride with dilute hydrochloric acid changed it almost completely into the anhydrous praseo-isomeride (Found: Co, 20·6%). The violeo-chloride was obtained also by allowing the filtrate in the preparation of (II) to evaporate slowly, small quantities of (II), (V), tris-ethylenediaminocobaltic chloride (XIII), and (XI) being removed, until the purplish-red hexagonal prisms of (I) separated; the crystals were violet when powdered. The plato-salt of (I) formed purple octahedra (Found: C, 11·6; H, 4·3; N, 13·5. Calc.: C, 11·5; H, 3·8; N, 13·4%).

The above chloride, $[Co\ en_3]Cl_3$ (XIII), prepared as its trihydrate by passing air through an aqueous solution of cobalt chloride and ethylenediamine, formed brownish-yellow prisms (Found: C, 18·2, 17·9; H, 7·6, 7·6; N, 20·9; Co, 15·0; H_2O, 13·5. Calc.: C, 18·0; H, 7·5; N, 21·0; Co, 14·8; H_2O, 13·5%), which readily lost the water at 110°; it formed a pale yellow plato-salt, $[Co\ en_3]_2(PtCl_4)_3$ (Found: C, 9·9; H, 3·6; N, 11·3. Calc.: C, 9·7; H, 3·2; N, 11·3%).

The compound (XI) was obtained by concentrating on the water-bath a solution of (XIII) (1 g.) and cobalt chloride (2 g.) in water (40 c.c.); it separated on cooling in yellowish-green needles, which were washed with alcohol and ether and dried over phosphoric oxide (Found: C, 16·6; H, 6·3; N, 19·2, 19·0; Cl, 31·9; Co, 20·0, 20·2. Calc. for $C_{12}H_{48}N_{12}Co_3Cl_8,3H_2O$: C, 16·5; H, 6·2; N, 19·2; Cl, 32·45; Co, 20·2%). The compound (X) was similarly obtained from a solution of (XIII) (1 g.) and cobalt chloride (4 g.) in dilute hydrochloric acid; the green crystals were washed and dried as above (Found: C, 14·2; H, 6·0; N, 16·6; Cl, 34·4; Co, 23·1. Calc.: C, 14·2; H, 5·5; N, 16·4; Cl, 34·7; Co, 23·1%). $[en\ H_2]_2CoCl_6$ was obtained in dark blue leaflets from cobalt chloride (10 g.) and ethylenediamine (5 g.) in 80 c.c. of 16% hydrochloric acid (Found: C, 12·3; H, 5·4; N, 14·2; Co, 14·9. Calc.: C, 12·1; H, 5·1; N, 14·1; Co, 14·9%). The *octachloride* (XII) was obtained by acidifying with hydrochloric acid an aqueous solution of the last chloride (1 part) and cobalt chloride (3 parts), and concentrating to half-bulk; addition of concentrated hydrochloric acid caused the separation of long pale blue prisms, which were washed with concentrated hydrochloric acid, alcohol, and ether, and dried over phosphoric oxide (Found: C, 13·6; H, 6·3; N, 16·0; Cl, 53·8; Co, 11·0. $C_6H_{30}N_6Cl_8Co$ requires C, 13·6; H, 5·7; N, 15·9; Cl, 53·7; Co, 11·15%).

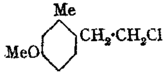
We thank the Chemical Society for a grant, and Messrs. The Mond Nickel Co. for the loan of platinum.

Queen Mary College (University of London). [*Received, February 5th*, 1937.]

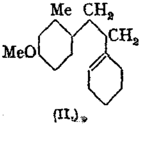
114. *Syntheses in the Phenanthrene Series. Part VI. 3-Methoxy-1-methylphenanthrene.*

By Peter Hill, W. F. Short, H. Stromberg, and A. E. Wiles.

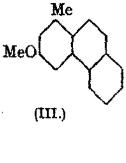
For the reason explained in Part V (this vol., p. 263) 3-*methoxy*-1-*methylphenanthrene* has been synthesised by two methods. In the first of these, interaction between the Grignard compound of 6-bromo-*m*-tolyl methyl ether and β-chloroethyl toluene-*p*-sulphonate afforded β-(5-*methoxy*-o-*tolyl*)*ethyl chloride* (I) in 36% yield. The pairing of the magnesium compound of (I) with *cyclo*hexanone produced 1-β-(5′-methoxy-*o*-tolyl)ethyl-*cyclo*hexanol, which was dehydrated to 1-β-(5′-*methoxy*-o-*tolyl*)*ethyl*-Δ¹-cyclo*hexene* (II). The synthesis of 3-methoxy-1-methylphenanthrene (III) was completed by treating the unsaturated compound with aluminium chloride and dehydrogenating the resulting mixture with sulphur.



(I.)

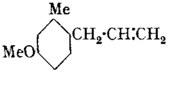


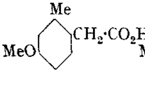
(II.)

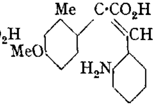


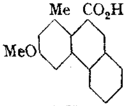
(III.)

In the alternative method, *6-allyl-*m*-tolyl methyl ether* (IV), prepared from allyl bromide and the Grignard compound of 6-bromo-*m*-tolyl methyl ether, was first oxidised to *5-methoxy-*o*-tolylacetic acid* (V). Condensation of the potassium salt of this acid with *o*-nitrobenzaldehyde furnished *2-nitro-α-(5′-methoxy-*o*-tolyl)cinnamic acid*, which was reduced to the *amino-acid* (VI). *3-Methoxy-1-methylphenanthrene-10-carboxylic acid* (VII) was obtained when the amino-acid was diazotised and warmed with alkali, and decarboxylation was smoothly effected by heating with copper powder. The resulting 3-methoxy-1-methylphenanthrene was demethylated to the corresponding phenol. *3-Hydroxy-1 methylphenanthrene*, its methyl ether, and the *picrate* of the latter melt at almost the same temperatures as the isomeric compounds obtained by the dehydrogenation of podocarpic acid (Sherwood and Short, *Rep. Austral. Assoc. Sci.*, **1933**, **31**, 38), but there is a considerable depression in melting point on admixture of the respective pairs.

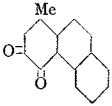

(IV.)

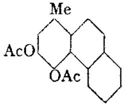

(V.)


(VI.)


(VII.)

3-Hydroxy-1-methylphenanthrene coupled with diazotised sulphanilic acid to produce a red dye and, owing to the fixation of the double bonds in the phenanthrene system, reaction doubtless occurred at position 4. Reduction of the dye with sodium hyposulphite furnished an unstable amino-phenol, which was successively oxidised (chromic anhydride) to *1-methylphenanthra-3 : 4-quinone* (VIII) and reduced by Thiele's method to *3 : 4-diacetoxy-1-methylphenanthrene* (IX).

(VIII.)



(IX.)

EXPERIMENTAL.

*6-Bromo-*m*-tolyl Methyl Ether.*—The bromination of *m*-cresol was effected as described by Darzens and Lévy (*Compt. rend.*, 1931, **193**, 292), but the phenol was dissolved in a mixture of acetic acid and chloroform (4 : 1 by vol.). The yield of 6-bromo-*m*-cresol, b. p. 120—131°/10 mm. (mostly at 123—125°/10 mm.), s. p. 48°, was 67% and methylation with methyl sulphate (1·3 mols.) in 10% sodium hydroxide solution afforded the phenol ether, b. p. 119—122°/18 mm., in 66% yield.

*β-(5-Methoxy-*o*-tolyl)ethyl Chloride* (I).—β-Chloroethyl toluene-*p*-sulphonate (1 mol.), dissolved in benzene (5·5 mols.), was added to a Grignard solution prepared from the preceding bromo-ether (1 mol.), magnesium (1 atom), and ether (6 mols.), and the mixture boiled for 3 hours. Decomposition with ice-cold dilute hydrochloric acid and careful fractionation afforded a 36% yield of *β-(5-methoxy-*o*-tolyl)ethyl chloride*, b. p. 134—135°/10 mm. (Found : Cl, 19·5. $C_{10}H_{13}OCl$ requires Cl, 19·25%).

*1-β-(5′-Methoxy-*o*-tolyl)ethyl-Δ^1-*cyclo*hexene* (II).—The aforesaid chloride (1 mol.) was slowly added to magnesium (3 atoms) and ether (15 mols.), the mixture boiled for ½ hour, and the liquid decanted from the excess of magnesium. *cyclo*Hexanone (1·9 mols.) was slowly added to the Grignard solution with mechanical stirring and cooling in a freezing mixture and, after 12 hours, the complex was decomposed with ice-cold ammonium chloride solution. Distillation afforded a fraction, b. p. 200—240°/20 mm., which deposited crystals, m. p. 87°, when dissolved in methyl alcohol and strongly cooled, and recrystallisation from acetone gave *αδ-di-(5-methoxy-*o*-tolyl)butane*, m. p. 89° (Found : C, 80·4; H, 8·5. $C_{20}H_{26}O_2$ requires C, 80·5; H, 8·7%). Removal of the methyl alcohol and distillation of the residue furnished a viscous liquid, b. p. 210—227°/23 mm., which still contained some of the butane derivative and was dehydrated by heating at 165° for 1 hour with 1½ parts of potassium hydrogen sulphate. Fractionation

afforded the cyclo*hexene* (II) in 22% yield as a colourless liquid, b. p. 192—195°/18 mm. (Found : C, 83·2; H, 9·4. $C_{16}H_{22}O$ requires C, 83·5; H, 9·6%).

6-*Allyl*-m-*tolyl methyl ether* (IV), b. p. 102—120°/10 mm., was obtained in 63% yield by adding allyl bromide (1·1 mols.) to a Grignard solution prepared from 6-bromo-*m*-tolyl methyl ether (1 mol.), magnesium (1 atom), and ether (5 mols.). A middle fraction, b. p. 107—108°/10 mm., was analysed (Found : C, 81·7; H, 8·7. $C_{11}H_{14}O$ requires C, 81·5; H, 8·6%).

5-*Methoxy*-o-*tolylacetic Acid* (V).—5% Potassium permanganate solution (6340 c.c.) was added with vigorous stirring to an emulsion of the preceding allyl compound (136 g.) in ice-water (500 c.c.) and glacial acetic acid (342 c.c.), cooled in a freezing mixture so that the temperature remained below 0°. Distillation with steam removed the unchanged allyl compound (45%) and the residue was made alkaline and filtered. The liquid was concentrated to 1 l. and acidified at 0°. The solid was exhaustively extracted with ligroin, and the extract recrystallised from the same solvent, giving long hexagonal plates, m. p. 106·5—107° (Found : C, 66·7; H, 6·7. $C_{10}H_{12}O_3$ requires C, 66·7; H, 6·7%). Yield, 15%. Extraction of the aqueous layer with ether gave acetic acid and a small quantity of 5-methoxy-*o*-toluic acid, which separated from acetic acid in long rods, m. p. 177—178°.

2-*Nitro*-α-(5′-*methoxy*-o-*tolyl*)*cinnamic Acid*.—The dry potassium salt (23 g.) of the preceding acid, *o*-nitrobenzaldehyde (16 g.), and acetic anhydride (83 c.c.) were maintained at 100° for 16 hours and then poured into hot water. The precipitate was warmed with sodium hydroxide solution and freed from neutral impurities by extraction with ether. When the crude acid, obtained by acidifying the alkaline layer, was extracted with chloroform, 0·5 g. of *o*-nitrocinnamic acid remained undissolved. Recrystallisation of the soluble portion from chloroform–light petroleum (b. p. 60—80°) gave a 27% yield of 2-*nitro*-α-(5′-*methoxy*-o-*tolyl*)*cinnamic acid*, which crystallised in radiating prisms, m. p. 169·5—170° (Found : C, 64·9; H, 4·9. $C_{17}H_{15}O_5N$ requires C, 65·2; H, 4·8%).

2-*Amino*-α-(5′-*methoxy*-o-*tolyl*)*cinnamic Acid* (VI).—The nitro-acid was reduced in the usual way with ferrous sulphate (7·7 mols.) and ammonia. The crude amino-acid is unstable and should be diazotised immediately. A portion of the crude *acid*, recrystallised from ligroin, formed small citron-yellow needles, m. p. 171—172° (Found : C, 72·2; H, 5·9. $C_{17}H_{17}O_3N$ requires C, 72·1; H, 6·0%).

3-*Methoxy*-1-*methylphenanthrene*-10-*carboxylic Acid* (VII).—Sodium nitrite solution (2 mols.) was rapidly added to a mechanically stirred suspension of the amino-acid in excess of dilute hydrochloric acid at 50°, and the mixture maintained at this temperature for ½ hour. Excess of urea was then added, the mixture filtered and the filtrate made alkaline and warmed at 90° for a few minutes. The solution was acidified at 0°, kept for 12 hours, and the solid collected. Recrystallisation from acetic acid furnished the *acid* in faintly coloured, long rods, m. p. 199—200° (Found : C, 76·8; H, 5·4. $C_{17}H_{14}O_3$ requires C, 76·7; H, 5·3%).

3-*Methoxy*-1-*methylphenanthrene* (III).—(1) Aluminium chloride (32 g.) was gradually added to an ice-cold solution of 1-β-(5′-methoxy-*o*-tolyl)ethyl-Δ^1-*cyclo*hexene (20 g.) in carbon disulphide (340 c.c.). After 12 hours at room temperature, the mixture was decomposed with ice-cold hydrochloric acid, and the carbon disulphide layer washed, dried, and evaporated. The residue (17 g.) was dehydrogenated at 180—240° with sulphur (6 g.) and distilled under diminished pressure. The distillate solidified and recrystallisation from alcohol furnished cream-coloured plates, m. p. 90°, of 3-*methoxy*-1-*methylphenanthrene* (Found : C, 86·3; H, 6·5. $C_{16}H_{14}O$ requires C, 86·5; H, 6·3%). The *picrate* separated from absolute alcohol in red needles, m. p. 147° (Found : C, 58·3; H, 3·85. $C_{22}H_{17}O_8N_3$ requires C, 58·5; H, 3·8%). (2) 3-Methoxy-1-methylphenanthrene-10-carboxylic acid (0·24 g.) was decarboxylated by heating at 230° for 1 hour with quinoline (1·2 c.c.) and copper powder (0·12 g.). The product melted at 90° after recrystallisation from alcohol and did not depress the m. p. of the methyl ether prepared by method (1). Demethylation of the phenol ether (0·2 g.) by boiling for 3½ hours with hydriodic acid (4 c.c., *d* 1·7) and acetic acid (4 c.c.) afforded 3-*hydroxy*-1-*methylphenanthrene*, which separated from benzene–light petroleum in almost white, radiating needles, m. p. 161° (Found : C, 86·3; H, 5·95. $C_{15}H_{12}O$ requires C, 86·5; H, 5·8%). This phenol gives a faint green colour with aqueous ferric chloride.

1-*Methylphenanthra*-3 : 4-*quinone* (VIII).—A solution of 3-hydroxy-1-methylphenanthrene (0·43 g.) in sodium hydroxide (0·74 g.) and water (5 c.c.) was added at 0° to a diazonium suspension prepared from sulphanilic acid (0·43 g.), and the mixture stirred for 10 minutes. The suspension of the red azo-dye was reduced by warming with a solution of sodium hyposulphite (1·0 g.), and the flocculent precipitate collected and extracted with two 10 c.c. portions of boiling dilute (1 : 1) hydrochloric acid containing sulphur dioxide. Addition of concentrated hydro-

chloric acid precipitated the amine hydrochloride as a white powder, m. p. *ca.* 210°, which rapidly turned brown in air. A solution of this hydrochloride (0·11 g.) in acetic acid (1·5 c.c.) was slowly added to an ice-cold solution of chromic anhydride (0·05 g.) in water (0·1 c.c.) and after being stirred for 10 minutes the solution was poured into water. The orange *quinone* was collected and washed with hot water. It decomposed at 300° without melting (Found: C, 80·8; H, 4·8. $C_{15}H_{10}O_2$ requires C, 81·1; H, 4·5%).

3 : 4-*Diacetoxy*-1-*methylphenanthrene* (IX).—The quinone (0·2 g.), dissolved in acetic anhydride (1·0 c.c.) and pyridine (3 drops), was stirred with zinc dust until the solution became pale yellow. The mixture was diluted with acetic acid (1·0 c.c.), filtered from excess of zinc, and diluted with water, and the solid collected. The *diacetate* separated from benzene–light petroleum in colourless plates, m. p. 138·5—139° (Found: C, 73·9; H, 5·3. $C_{19}H_{16}O_4$ requires C, 74·0; H, 5·2%).

We are indebted to the Chemical Society for a grant and to Imperial Chemical Industries Ltd. (Dyestuffs Group) for various gifts of chemicals.

THE COLLEGE OF TECHNOLOGY, MANCHESTER. [*Received, January 20th, 1937.*]

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115. *Anisoxide. Part I.*

By R. W. JACKSON and W. F. SHORT.

DURING a re-examination of star aniseed oil (from *Illicium verum*) carried out by one of us in conjunction with Mr. C. B. Radcliffe, M.Sc., in 1932, a new constituent was isolated. We have now studied the reactions of this compound, for which we suggest the name *anisoxide*.

The new compound was isolated from the oil by protracted fractionation with an efficient column and was concentrated in the fraction, b. p. 135—145°/12 mm., which was then heated with sodium–potassium alloy to destroy active oxygenated constituents. Further fractionation afforded a portion, b. p. 138—143°/12 mm., which solidified (m. p. 36—38°). The solid was excessively soluble in the usual organic solvents, but could be recrystallised from ice-cold methyl alcohol, separating in large white cubic crystals, m. p. 41°, having a faint but characteristic odour. It could be distilled unchanged at atmospheric pressure, but on exposure to air rapidly changed to a viscous yellow liquid with production of a pungent odour. The average content of anisoxide in the three specimens of star aniseed oil examined was 0·2%.

Owing to the ease with which anisoxide yields acetaldehyde, persistently low values for carbon were obtained until special precautions were adopted in the analyses. Results agreeing with the formula $C_{14}H_{18}O$ were then obtained and this composition was substantiated by analyses of the hydro-derivatives (below).

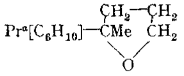
Anisoxide is a cyclic ether, since it is inert towards the usual reagents for alcohols and carbonyl compounds and contains no methoxy- or ethoxy-group. It is highly unsaturated, imparting a deep red colour to tetranitromethane in chloroform solution, but no solid compounds could be obtained with the usual olefinic addenda. The high molecular refraction, $[R_L]_D$ 65·66 (calc. for an aliphatic oxide $C_{14}H_{18}O|\overline{_5}$, 63·96, and for a monocyclic oxide $C_{14}H_{18}O|\overline{_4}$, 62·23), indicates that the oxide contains either conjugated ethylenic linkages or an acetylenic linkage. The presence of conjugated double bonds was proved by (1) the formation of an *addition compound*, $C_{18}H_{20}O_4$, with maleic anhydride, (2) reduction to *dihydroanisoxide*, $C_{14}H_{20}O$, with sodium and alcohol. The dihydro-compound is stable towards further reduction with these reagents and exhibits a smaller exaltation in its molecular refraction.

An attempt to determine the degree of unsaturation by perbenzoic acid titration was frustrated by the slowness of the reaction, only 1·5 atoms of oxygen being absorbed in 300 hours. Energetic catalytic reduction, however, produced *perhydroanisoxide*, $C_{14}H_{26}O$, still containing the oxide ring and giving no colour with tetranitromethane.

Anisoxide afforded 2 mols. of acetic acid on oxidation by the Kuhn–Roth micro-method (chromic anhydride) and one of these is derived from an ethylidene group, since oxidation

of anisoxide with moist air at 70° or with dilute ozone in aqueous suspension produces acetaldehyde, which was characterised as aldomedon. The double bond of the ethylidene group is probably conjugated, since dihydroanisoxide does not yield acetaldehyde on oxidation.

In order to determine the nature of the oxide ring, experiments were made with perhydroanisoxide, since anisoxide is resinified by acids and halogens. Perhydroanisoxide was recovered unchanged after treatment with phenylmagnesium bromide at 100°, so the presence of a 1 : 2- or 1 : 3-oxide ring is improbable (Blaise, *Compt. rend.*, 1902, **134**, 553; Grignard, *Bull. Soc. chim.*, 1903, **29**, 944). When perhydroanisoxide was heated with hydrogen bromide in acetic acid, the oxide ring was opened with production of an unstable *dibromide*, $C_{14}H_{26}Br_2$. Digestion with aniline produced an unsaturated *hydrocarbon*, $C_{14}H_{24}$, which was oxidised by ozone to a *ketone*, $C_{11}H_{20}O$, characterised by the preparation of a *semicarbazone*, m. p. 161—162°. Oxidation of this ketone with sodium hypoiodite gave iodoform and it is therefore evident that perhydroanisoxide must be represented by (I) and the ketone $C_{11}H_{20}O$ by (II).

(I.) 

$Pr^a[C_6H_{10}]—COMe$ (II.)

Anisoxide clearly does not belong to the furan group represented by carlina oxide, perillene, elsholtzione and menthofuran, but is a hydrofuran derivative. In agreement with this, no pyrrole reactions were exhibited by the product obtained by heating anisoxide to 200° with alcoholic ammonia.

Oxidation of anisoxide with potassium permanganate in pyridine solution gave an *acid*, $C_{12}H_{14}O_3$, m. p. 182°, evidently produced by oxidation of the ethylidene group:

$$[C_{11}H_{13}O]\cdot CH{:}CHMe \longrightarrow [C_{11}H_{13}O]\cdot CO_2H$$

On further oxidation it afforded first an *acid*, $C_{11}H_{12}O_3$, m. p. 215—216°, and then an *acid*, $C_{11}H_{10}O_4$, m. p. 179·5—180·5°; the latter is a hydroxy-acid, since the *methyl* ester furnished one molecule of methane on reaction with methylmagnesium iodide. Finally, oxidation of dihydroanisoxide with either potassium permanganate or ozone produced a liquid ketone, $C_{14}H_{18}O_2$, characterised by its *semicarbazone*, m. p. 191·5—192·5°. The bearing of these results on the structural problem is reserved for discussion in a subsequent communication.

Takens (*Reichstoffind.*, 1929, **4**, 8) records the presence in fennel oil and star anise oil of a compound, m. p. 21·5°, isomeric with anisoxide. This substance, however, is stated to yield *p*-anol, CHMe:CH·C_6H_4·OH, on distillation at atmospheric pressure and its physical constants are different from those of anisoxide.

The final fraction of star aniseed oil contains, in addition to anisic acid, a small quantity of a paraffin hydrocarbon, $C_{19}H_{40}$, m. p. 45—46°.

Experimental.

Anisoxide.—The pure *oxide* consists of cubic crystals, m. p. 41°, b. p. 140°/11 mm., $d_{4^\circ}^{50^\circ}$ 0·9604, $n_D^{50^\circ}$ 1·5361, α_D ± 0° (Found: C, 82·8; H, 8·9. $C_{14}H_{18}O$ requires C, 83·2; H, 8·9%). Anisoxide (1·0 g.) and maleic anhydride (0·5 g.) were heated at 170° for ½ hour, and the product washed with alcohol and recrystallised from acetic acid. Microscopic prisms of an *addition compound* decomposing at 280° were obtained (Found: C, 72·1; H, 6·7. $C_{18}H_{20}O_4$ requires C, 72·0; H, 6·7%).

Reduction of Anisoxide.—(i) *Catalytic.* The oxide (50 g.) in acetic acid (1 l.) and platinum oxide (7·5 g.) were shaken in hydrogen at a pressure of 40 lb. per sq. in., and the catalyst reactivated at intervals by shaking with air. Absorption ceased after 26·5 l. of hydrogen (4·8 mols.) had been absorbed. *Perhydroanisoxide* (49·5 g.), isolated in the usual manner, was a colourless mobile oil, b. p. 120—122°/10 mm., $d_{4^\circ}^{25^\circ}$ 0·8999, $n_D^{25^\circ}$ 1·4656, $[R_L]_D$ 64·66 (calc. for $C_{14}H_{26}O$, 64·10) (Found: C, 79·9; H, 12·6. $C_{14}H_{26}O$ requires C, 80·0; H, 12·4%). Perhydroanisoxide gives no colour with tetranitromethane and does not react with 3 : 5-dinitrobenzoyl chloride.

(ii) ***With sodium and alcohol.*** Sodium (16·4 g.) was added as rapidly as possible to a boiling solution of anisoxide (10 g.) in ethyl alcohol (75 c.c.), the reaction being completed by heating to 120° and slowly adding more alcohol (100 c.c.). After removal of the alcohol in steam, the oil was extracted with ether, the ether dried and evaporated, and the residue distilled under diminished pressure; *dihydroanisoxide* (9 g.) was obtained as a colourless oil, b. p. 120—122°/10 mm., $d_{4°}^{25°}$ 0·9501, $n_{D}^{25°}$ 1·5073, $[R_L]_D$ 64·00 (calc. for $C_{14}H_{20}O\overline{|_3}$, 62·69) (Found : C, 82·3, 82·3; H, 10·0, 10·0. $C_{14}H_{20}O$ requires C, 82·4; H, 9·8%).

Oxidation of Anisoxide.—(i) *With air.* Air was aspirated through a suspension of anisoxide (0·5 g.) in water (10 c.c.) at 40—45°. The issuing vapour gave a positive test for acetaldehyde with piperidine and sodium nitroprusside (Rimini, *Z. anal. Chem.*, 1904, **43**, 517) and when it was passed for 8 hours through a solution of 5 : 5-dimethyl*cyclo*hexane-1 : 3-dione (0·6 g. in 10 c.c. of water) a precipitate separated after keeping for 12 hours. The solid had m. p. 140° after recrystallisation from dilute ethyl alcohol (free from acetaldehyde) and did not depress the m. p. (140°) of authentic aldomedon (Neuberg and Reinfurth, *Biochem. Z.*, 1920, **106**, 286).

(ii) *With ozone.* Ozonisation of anisoxide in 70% acetic acid (4 vols.) with 5% ozone for 8 hours at 0°, decomposition of the ozonide with ice-water, and distillation of the liquid furnished acetaldehyde (aldomedon, m. p. and mixed m. p. 140°) and resinous compounds.

(iii) *With chromic anhydride.* Oxidation of anisoxide (13·5 mg.) under the conditions specified by Kuhn and Roth (*Ber.*, 1933, **66**, 274) afforded distillates which neutralised 10·8 and 11·4 ml. of 0·01*N*-sodium hydroxide solution, equivalent to 1·6 and 1·7 mols. of acetic acid respectively.

(iv) *With potassium permanganate.* The same acid (A) was produced when the oxidation was conducted in acetone or water, but the best yields (64%) were obtained in pyridine solution. Potassium permanganate solution (2% : equivalent to 4 atoms of oxygen) was added drop by drop to a mechanically stirred solution of anisoxide in pyridine (30 vols.) at 0°. After 14 hours, the manganese dioxide was removed by filtration and washed with boiling water and the concentrated filtrates were acidified at 0°. The *acid* (A) was purified by conversion into the sodium salt and crystallisation from ligroin, from which it separated in rectangular plates, m. p. 181—182° (Found : C, 69·85; H, 6·7; *M*, by titration, 203. $C_{12}H_{14}O_3$ requires C, 69·9; H, 6·8%; *M*, 206). The *anilide*, prepared by the successive action of thionyl chloride and aniline, crystallised from ligroin in rhombic plates, m. p. 155—156° (Found : C, 75·5; H, 6·8; N, 5·0. $C_{18}H_{19}O_2N$ requires C, 76·6; H, 6·8; N, 5·0%).

Oxidation of the Acid (A).—Aqueous potassium permanganate (2%, 160 c.c.) was slowly added to a stirred solution of the acid A (1·5 g.) in dilute sodium carbonate solution (10 c.c.). After 8 hours the filtered sludge was repeatedly digested with water and the combined washings were concentrated and acidified. The *acid* (B) (yield, 55%) crystallised from dilute acetic acid in long needles, m. p. 215—216° (Found : C, 69·55; H, 5·5. $C_{11}H_{10}O_3$ requires C, 69·5; H, 5·2%).

Oxidation of the Acid (B).—Oxidation of the acid B (1·7 g.) in dilute sodium carbonate solution with 2% potassium permanganate solution (190 c.c.) was complete in 10 hours and afforded an *acid* (C), which crystallised from ligroin in clusters of large plates, m. p. 179·5—180·5° (Found : C, 64·0; H, 5·0. $C_{11}H_{10}O_4$ requires C, 64·1; H, 4·8%). The *methyl* ester crystallised from benzene in well-defined plates, m. p. 79—80° (Found : C, 65·7, 65·6; H, 5·7, 5·3. $C_{12}H_{12}O_4$ requires C, 65·5; H, 5·4%). A Zerewitinoff determination showed that the acid (C) contains one hydroxyl group; 0·100 g. of its methyl ester evolved 11·0 c.c. of methane at 15°/758 mm., equivalent to 1·03 atoms of active hydrogen per molecule.

Fission of the Oxide Ring in Perhydroanisoxide.—Perhydroanisoxide (5 c.c.), acetic acid (5 c.c.), and hydrogen bromide–acetic acid (50%; 5 c.c.) were heated at 100° in a sealed tube for 2 hours and the liquid, which had separated into two layers, was poured into water and extracted with ether. The solution was washed with dilute aqueous sodium carbonate, dried, and evaporated. The residual *dibromide* (Found : Br, 42·9. $C_{14}H_{26}Br_2$ requires Br, 45·2%) was a heavy oil which would not solidify and could not be distilled without decomposition. A mixture of the dibromide (5 g.) and aniline (20 c.c.) was warmed cautiously and, after the exothermal reaction had subsided, was boiled for ½ hour. The mixture was then acidified and distilled in steam, and the colourless oil collected in ether. The *unsaturated hydrocarbon* (2·3 g.) had b. p. 110—112°/10 mm. (Found : C, 87·0; H, 13·2. $C_{14}H_{24}$ requires C, 87·5; H, 12·5%).

Oxidation of the Unsaturated Hydrocarbon, $C_{14}H_{24}$, *with Ozone.*—The hydrocarbon (25 g.) in acetic acid (150 g.), cooled in ice, was ozonised for 8 hours, and the ozonide decomposed by boiling the solution for ½ hour. After most of the acetic acid had been removed by distillation under diminished pressure, the liquid was poured into water, and the neutral products (13 g.) separated from acids (8·5 g.). The acids were esterified with methyl alcohol and distilled,

yielding an ester fraction, b. p. 135—140°/5 mm. (5·0 g.; equiv., 214), which was hydrolysed to a mixture of acids (3·0 g.), b. p. 175—190°/10 mm., from which no homogeneous substance could be isolated. Fractionation of the neutral product afforded a *ketone* (1·5 g.), b. p. 102—105°/10 mm. (Found: C, 77·9; H, 10·2. $C_{10}H_{20}O$ requires C, 78·5; H, 11·9%). The new ketone was converted into the *semicarbazone*, which crystallised from methyl alcohol in microscopic prisms, m. p. 161—162° (Found: C, 64·0; H, 10·0; N, 18·6. $C_{12}H_{23}ON_3$ requires C, 64·0; H, 10·0; N, 18·7%). When the ketone was treated with Fuson's reagent (*J. Amer. Chem. Soc.*, 1934, **56**, 1638), iodoform, m. p. and mixed m. p. 119—120°, was produced.

Oxidation of Dihydroanisoxide.—(i) *With potassium permanganate.* The oxide (7·5 g.) in pyridine (75 c.c.) was stirred, and 2% potassium permanganate solution (315 c.c.) added during 10 hours. The manganese dioxide was removed and washed with boiling water. The filtrates were acidified and extracted continuously with ether, and the extract washed with dilute sodium hydroxide solution to remove traces of acids. After removal of the ether, distillation under diminished pressure (10 mm.) afforded the following fractions: (1) 125—135° (2 g.); (2) 135—200° (1 g.). Fraction (1) consisted of dihydroanisoxide, and fraction (2) furnished a *semicarbazone* which separated from benzene-ligroin in small rods, m. p. 191·5—192·5° (Found: C, 65·4; H, 7·2; N, 15·4. $C_{15}H_{21}O_2N_3$ requires C, 65·4; H, 7·6; N, 15·3%). Fraction (2) did not reduce Tollens's reagent and therefore contains a ketone, $C_{14}H_{18}O_2$.

(ii) *With ozone.* Dihydroanisoxide (6 g.) in acetic acid (30 c.c.), cooled in ice, was ozonised for 8 hours, and the ozonide decomposed by boiling for ½ hour. The acid product had b. p. 125—200°/4 mm. (0·2 g.) and the neutral product consisted of dihydroanisoxide, b. p. 123—130°/10 mm. (0·8 g.), and a portion, b. p. 130—160°/10 mm. (0·8 g.), which afforded a semicarbazone, m. p. 191·5—192°, identical with that obtained by method (1).

The Paraffin Hydrocarbon, $C_{19}H_{40}$.—The final fraction, b. p. 160—186°/5 mm., obtained in the distillation of star aniseed oil deposited crystals. These were acidic and after recrystallisation from hot water had m. p. 184° both alone and after admixture with anisic acid. The oily portion of the fraction was washed with alkali and distilled from sodium under diminished pressure. The distillate deposited a wax-like solid, which crystallised from chloroform-methyl alcohol in white flakes, m. p. 45—46° (Found: C, 85·2, 85·2; H, 14·8, 14·8; *M*, cryoscopic in camphor, 264, 266. $C_{19}H_{40}$ requires C, 85·1; H, 14·9%; *M*, 268). The *hydrocarbon* behaves as a saturated compound with tetranitromethane, bromine, and potassium permanganate.

We are deeply indebted to Messrs. A. Boake Roberts & Co. of Stratford for the gift of the star aniseed oil used in this research.

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116. *Totarol. Part I.*

By W. F. SHORT and H. STROMBERG.

THE dextrorotatory diterpene alcohol, totarol, m. p. 127°, was first isolated by Easterfield and McDowell (*Trans. New Zealand Inst.*, 1911, **43**, 55; 1915, **48**, 518) from the wood of the totara tree (*Podocarpus totara*). We have been encouraged by Professor Easterfield to continue the work which he initiated and the present communication describes an investigation on the structure of totarol. Easterfield proposed the formula $C_{20}H_{30}O$, and concluded that the compound is an alcohol, since it was neutral and afforded a crystalline acetate. The compound was believed to be a tertiary alcohol, since it was acetylated slowly.

Although the melting point of totarol has been raised to 132°, the analytical figures still agree with the formula $C_{20}H_{30}O$ and this is fully confirmed by an examination of the derivatives of totarol. The alcohol was converted into a *formate*, $C_{21}H_{30}O_2$, m. p. 125·5°, by boiling with concentrated formic acid, and remained unchanged when heated with phosphoric oxide in xylene solution or with phthalic anhydride in benzene solution. Phthalic anhydride at 140°, however, converted totarol into a *hydrogen phthalate*, m. p. 161—163°, and it may therefore be concluded that the alcoholic group is secondary.*

* Oxidation experiments will be reported in a subsequent communication.

Totarol is unsaturated, since it gives a red colour with tetranitromethane and absorbs bromine very rapidly. The molecular refraction was determined in quinoline and acetophenone solution, since Krollpfeiffer (*Annalen*, 1923, **430**, 161) has shown that these solvents have the smallest influence on the molecular refraction of a dissolved substance and they have already been successfully applied in the resin acid series (Sherwood and Short, *Rep. Austral. Assocn. Sci.*, 1933, **31**, 33). The results agreed with the conclusion that totarol is tricyclic and contains three ethylenic linkages. A quantitative study of the action of perbenzoic acid upon totarol and *totaryl methyl ether*, m. p. 92—92·5°, prepared by the action of methyl iodide upon potassium totaryl oxide, also showed the presence of three unsaturated linkages.

Totarol is resistant to catalytic reduction, and hydrogenation was effected in acetic acid solution at 70° in presence of palladium–charcoal with hydrogen at a pressure of 30 lb. per sq. in. The product consisted of a saturated lævorotatory *hydrocarbon* (*totarane*), $C_{20}H_{36}$, m. p. 74·5—75°, and a smaller quantity of *dihydrototarol*, $C_{20}H_{32}O$, m. p. 151°. The dihydro-compound was slowly reduced by the catalytic method to *tetrahydrototarol*, $C_{20}H_{34}O$, m. p. 134·5°, but attempts to obtain the saturated alcohol $C_{20}H_{36}O$ have so far been unsuccessful. It is improbable that the ethylenic linkages in totarol are conjugated, since the alcohol does not react with maleic anhydride, neither is it reduced by sodium in ethyl- or amyl-alcoholic solution.

Dehydrogenation of totarol with selenium at 320° afforded a 70% yield of a *phenol*, $C_{15}H_{12}O$, m. p. 191°, which furnished a *methyl ether*, m. p. 133°, and an *acetate*, m. p. 136°. The methyl ether united with picric acid to form an unstable picrate and it was concluded that the phenol $C_{15}H_{12}O$ is a hydroxymethylphenanthrene; this conclusion was confirmed by the preparation of an orange-yellow *quinone*, $C_{17}H_{12}O_4$ (*quinoxaline*, m. p. 244·5—246·5°), by the oxidation of the acetate. When the phenol was distilled with zinc dust, 1-methylphenanthrene was obtained, so this compound must be a 1-methylphenanthrol. The hydroxyl group cannot reside at position 9 or 10, and positions 2, 4, 5 and 7 were apparently excluded by the observation that the corresponding 9 : 10-quinone did not give the reversible colour reaction stated by Fieser and Young (*J. Amer. Chem. Soc.*, 1931, **53**, 4126) to be characteristic of hydroxyphenanthra-9 : 10-quinones containing a hydroxyl group in the *m*-position to either of the carbonyl groups. Position 8 was excluded, since the hydroxy-quinone did not yield a coloured ester with boroacetic anhydride (Dimroth, *Ber.*, 1921, **54**, 3020; *Annalen*, 1926, **445**, 97, 123). Syntheses of 3- and 6-hydroxy-1-methylphenanthrene were effected (this vol., p. 510, and forthcoming publication), but neither was identical with the compound obtained from totarol. Of the remaining positions, 7 appeared to be the most probable on phyto-chemical grounds and a synthesis of 7-hydroxy-1-methylphenanthrene (J., 1936, 319) showed that this substance is identical with the phenol obtained from totarol. It is therefore clear that Fieser's colour reaction is not invariably diagnostic. 7-Hydroxy-1-methylphenanthrene is also produced by the dehydrogenation of totarol with sulphur or with palladium–charcoal.

An attempt was made to determine the way in which five carbon atoms of totarol are eliminated by an analysis of the gases produced during the catalytic dehydrogenation, but was rendered abortive by resinification and inconstancy in composition. The gas evolved was therefore partly condensed in liquid air and the temperature of the liquid was then allowed to rise slowly. The liquid phase persisted almost up to the boiling point of propane (− 46·5°), so totarol probably contains an *iso*propyl group, which is eliminated during dehydrogenation. In this connection, the dehydrogenation of totarane afforded interesting results. The product was a phenanthrene *hydrocarbon*, $C_{18}H_{18}$, m. p. 102°, which yielded a *quinone*, m. p. 160·5—161·5°, and a *quinoxaline*, m. p. 154—154·5°, and was oxidised by alkaline potassium ferricyanide to a *phenanthrenedicarboxylic acid*, $C_{16}H_{10}O_4$, isolated as its *methyl* ester, m. p. 136°. In view of the fact that totarol contains a methyl group in position 1, and of the elimination of propane during the dehydrogenation of the alcohol, it seems probable that this hydrocarbon is a 1-methyl-*x*-*iso*propylphenanthrene, but it is different from the three isomers known at present. It is also clear that an alkyl migration must occur either during the transformation of totarol into totarane or during the dehydrogenation.

The research is being actively pursued and the structural problem will be reviewed in a subsequent communication.

EXPERIMENTAL.

Totarol.—The crude alcohol was purified by distillation and by crystallisation of the fraction, b. p. 205—239°/10 mm., from ligroin. It crystallised in clustered needles, m. p. 132°, and had $[\alpha]_D^{20°}$ + 41·34° in 4% alcoholic solution (Found: C, 83·9; H, 10·4. Calc. for $C_{20}H_{30}O$: C, 83·9; H, 10·5%). An 11·11% solution of totarol in quinoline ($d_{4°}^{24·6°}$ 1·0819, $n_D^{24·6°}$ 1·6168) had $d_{4°}^{24·6°}$ 1·0778, $n_D^{24·6°}$ 1·6110 and an 8·38% solution in acetophenone ($d_{4°}^{24·6°}$ 1·02495, $n_D^{24·6°}$ 1·5313) $d_{4°}^{24·6°}$ 1·0264, $n_D^{24·6°}$ 1·5337, whence $[R_L]_D$ = 87·63 (in quinoline) and 88·98 (in acetophenone). $C_{20}H_{30}O\,|\!\overline{=}_3$ requires $[R_L]_D$ 88·08. With perbenzoic acid, the alcohol absorbed oxygen equivalent to 3·15, 3·15 ethylene linkages.

Totaryl Formate.—A mixture of totarol (5 g.) and 98% formic acid (60 c.c.) was boiled for 2 hours, poured into ice-water, neutralised with dilute sodium hydroxide solution, and extracted with ether. The residue obtained by evaporating the dry solution was recrystallised from alcohol, which deposited hexagonal prisms, m. p. 125·5° (Found: C, 79·95; H, 9·35. $C_{21}H_{30}O_2$ requires C, 80·3; H, 9·55%).

Totaryl Acetate.—Concentrated sulphuric acid (2 drops) was added to a solution of totarol (19·2 g.) in acetic anhydride (148 c.c.), and the mixture boiled for 1 hour. Acetic anhydride was destroyed by warming with water, and the precipitate recrystallised from ethyl alcohol. The *acetate* consisted of rectangular plates, m. p. 121·5° (Found: C, 80·3; H, 9·8. $C_{22}H_{32}O_2$ requires C, 80·5; H, 9·75%), and had $[\alpha]_D^{18°}$ + 44·58° in 4% solution in ether. Hydrolysis with 10% methyl-alcoholic potash afforded totarol, so no isomerisation had been caused by the acid reagents.

Totaryl Hydrogen Phthalate.—Totarol was heated at 140° for 6 hours with an equal weight of phthalic anhydride. The mixture was extracted with ether, and the extract filtered to remove phthalic anhydride and shaken with sodium hydroxide solution. The solid obtained on acidification was extracted with chloroform, filtered from undissolved phthalic acid, and recrystallised from alcohol. *Totaryl hydrogen phthalate* was obtained in small prisms melting somewhat indefinitely at 161—163° (Found: C, 77·0; H, 7·5. $C_{28}H_{34}O_4$ requires C, 77·4; H, 7·8%). Hydrolysis with 2*N*-alcoholic potash afforded totarol.

Totaryl Methyl Ether.—Methyl iodide (40 c.c.) was added to a suspension of potassium totaryl oxide, prepared from the metal (2·4 g.), totarol (7·2 g.), benzene (140 c.c.), and xylene (70 c.c.) heated at 70° for 2 hours, and the mixture boiled for 2 hours. Alcohol (20 c.c.) was then added, and the mixture diluted with a large volume of ether. The solution was washed, dried, and evaporated. Recrystallisation from chloroform–ethyl alcohol afforded small rhombs, m. p. 92—92·5°, $[\alpha]_D^{18°}$ + 41·95° (4% solution in ether), of *totaryl methyl ether* (Found: C, 83·7; H, 10·3. $C_{21}H_{32}O$ requires C, 84·0; H, 10·7%). Yield, 82%. With perbenzoic acid, the ether absorbed oxygen equivalent to 2·95 and 2·85 ethylene linkages.

Reduction of Totarol.—Totarol and totaryl acetate in acetic acid or alcohol could not be reduced in presence of Adams's platinum oxide catalyst at 20—70° and at pressures up to 3 atmospheres. Palladium–strontium carbonate also was ineffective as a catalyst, but reduction was smoothly effected in presence of 10% palladium–charcoal. The alcohol (4·8 g.) in acetic acid (50 c.c.) was shaken with hydrogen in the presence of palladium–charcoal (1·6 g.), 1045 c.c. (2·8 mols.) of hydrogen being absorbed in 6 hours at 70° at a pressure of 30 lb. per sq. in. (at atmospheric pressure, the same quantity of hydrogen is absorbed after 36 hours at 70—80°). The hot solution was filtered, the solvent removed by distillation under diminished pressure, and the residue dissolved in the minimum quantity of ethyl acetate. The solution deposited an impure hydrocarbon, m. p. 80—82°, and recrystallisation from methyl alcohol furnished thick plates of *totarane* (2·5 g.), m. p. 74·5—75° (Found: C, 86·7; H, 12·9. $C_{20}H_{36}$ requires C, 87·0; H, 13·0%). The hydrocarbon gave no colour with tetranitromethane and had $[\alpha]_D^{20°}$ − 31·06° in 4% ethereal solution. Evaporation of the ethyl acetate afforded *dihydrototarol* (1·6 g.), which crystallised from ligroin in clustered plates, m. p. 151—151·5°, $[\alpha]_D^{20°}$ + 20·13° in 4% ethereal solution (Found: C, 83·1; H, 10·9. $C_{20}H_{32}O$ requires C, 83·3; H, 11·1%). This alcohol gave a pale yellow colour with tetranitromethane and when digested with formic acid afforded *dihydrototaryl formate*, which crystallised from methyl alcohol in plates, m. p. 104·5—105° (Found: C, 80·0; H, 10·2. $C_{21}H_{32}O_2$ requires C, 79·8; H, 10·1%).

Tetrahydrototarol.—Dihydrototarol was not reduced in ethyl alcohol or ethyl acetate at 70° and 2 atmospheres in presence of palladium–charcoal, but reduction took place in acetic acid. A mixture of dihydrototarol (1·0 g.), palladium–charcoal (0·3 g.) and acetic acid (50 c.c.) was

shaken in hydrogen until absorption ceased, filtered hot, and evaporated under diminished pressure. A hot saturated solution of the residue in ethyl acetate deposited a little dihydrototarol and crystallisation of the soluble portion from ligroin furnished elongated rectangular prisms of *tetrahydrototarol*, m. p. 134·5° (Found: C, 82·3; H, 11·7. $C_{20}H_{34}O$ requires C, 82·7; H, 11·7%). This compound gave a faint yellow colour with tetranitromethane.

Dehydrogenation of Totarol.—(i) *With selenium.* Totarol (15 g.) and selenium powder (30 g.) were heated at 310—320° for 34 hours and the cold mixture was dissolved in acetone, boiled with charcoal, and evaporated. The residue was dissolved in hot sodium hydroxide solution, filtered, and reprecipitated with acid. Recrystallisation from benzene afforded small clustered needles, m. p. 190—191° (Found: C, 86·3; H, 5·85. $C_{15}H_{12}O$ requires C, 86·5; H, 5·7%). The mother-liquors were diluted with ether and washed with alkali, and the solution dried and evaporated. Distillation of the residue from sodium afforded a colourless oil (0·6 g.), b. p. 155—160°/4 mm., which soon solidified. The crude hydrocarbon was purified by conversion into its picrate and warming with ammonia. The regenerated hydrocarbon (0·02 g.) melted at 118° and, when mixed with picric acid (0·02 g.) in alcohol, furnished a picrate which melted at 134·5° either alone or after admixture with authentic 1-methylphenanthrene picrate. The same hydrocarbon (0·14 g.) was also obtained by heating a mixture of the phenol $C_{15}H_{12}O$ (0·5 g.) with zinc dust (13 g.) and allowing the vapours to pass through a 20 cm. layer of hot zinc dust. The hydrocarbon and its picrate did not depress the m. p.'s of 1-methylphenanthrene and its picrate.

(ii) *With sulphur.* A mixture of totarol (3 g.) and sulphur (3 g.) was heated at 180—260° for 5 hours and then distilled at 4 mm. In this way, 1·2 g. of the phenol, m. p. 190—191°, were obtained, but no appreciable quantity of hydrocarbon was produced.

(iii) *Catalytic.* A mixture of totarol (3 g.) and 10% palladium–charcoal (2 g.) was heated for 6¼ hours at 310—330° and for 3 hours at 350—360°. The volume of gas evolved was 1245 c.c. and 0·4 g. of the phenol $C_{15}H_{12}O$ and 0·04 g. of 1-methylphenanthrene (picrate, m. p. 133·5°) were isolated from the residue.

Investigation of the Phenol $C_{15}H_{12}O$.—Methylation of the phenol (0·2 g.) with sodium hydroxide (0·15 g.), water (1 c.c.), and methyl sulphate (0·5 c.c.) at 60° furnished a *methyl* ether, which crystallised from alcohol in white plates, m. p. 133·5—134·5° (Found: C, 86·2; H, 6·5. $C_{16}H_{14}O$ requires C, 86·5; H, 6·3%). When the phenol (0·3 g.), acetic anhydride (3·4 g.), and sodium acetate (0·1 g.) were boiled for 1 hour, the *acetate*, m. p. 133·5—136°, was obtained in 87% yield (Found: C, 81·4; H, 5·6. $C_{17}H_{14}O_2$ requires C, 81·6; H, 5·6%). Oxidation of the acetate (0·5 g.) in acetic acid (7·5 c.c.) with chromic anhydride (0·6 g.) in water (1 c.c.) and acetic acid (2·5 c.c.) at 50—60° furnished an orange-yellow *quinone*, which crystallised from glacial acetic acid in rhombic plates, m. p. 207° (decomp.) (Found: C, 72·7; H, 4·9. $C_{17}H_{12}O_4$ requires C, 72·85; H, 4·3%). The quinone (0·133 g.) in the minimum amount of acetic acid and *o*-phenylenediamine (0·062 g.) in alcohol (1·5 c.c.) afforded a *quinoxaline*, which separated from alcohol–chloroform in long yellow needles (0·13 g.), m. p. 244·5—245·5° (Found: C, 78·65; H, 4·65. $C_{23}H_{16}O_2N_2$ requires C, 78·4; H, 4·5%) The acetoxy-quinone (0·02 g.) was hydrolysed by trituration with 2*N*-aqueous alcoholic sodium hydroxide, and the product precipitated with acid and recrystallised from alcohol. The *hydroxy-quinone* separated in small clustered needles, m. p. 228° (decomp.) (Found: C, 75·2; H, 4·5. $C_{15}H_{10}O_3$ requires C, 75·6; H, 4·2%). The hydroxy-quinone formed a deep indigo-blue solution in dilute aqueous potassium hydroxide, but the colour remained unchanged on warming. The phenol $C_{15}H_{12}O$ did not depress the m. p. of synthetic 7-hydroxy-1-methylphenanthrene and there was no depression when the respective acetates and methyl ethers were mixed.

Dehydrogenation of Totarane.—This hydrocarbon was recovered unchanged after heating at 310—320° for 18 hours with selenium. Dehydrogenation of totarane (0·9 g.) with 10% palladium–charcoal for 4 hours at 300—340° afforded 420 c.c. of gas and extraction of the residue with ether furnished a crystalline *hydrocarbon*, which was purified through its picrate and crystallised from alcohol in thick plates (0·15 g.), m. p. 101·5—102° (Found: C, 92·3; H, 7·4. $C_{18}H_{18}$ requires C, 92·3; H, 7·7%). The *picrate* crystallised from alcohol in golden-yellow needles, m. p. 142·5° (Found: C, 62·3; H, 4·7. $C_{18}H_{18},C_6H_3O_7N_3$ requires C, 62·2; H, 4·5%). Oxidation of the hydrocarbon (0·2 g.) in acetic acid (3 c.c.) with chromic anhydride (0·26 g. in 0·5 c.c. of water and 1·5 c.c. of acetic acid) at 50—60° afforded the *quinone*, which crystallised in long rods, m. p. 160·5—161·5° (Found: C, 81·5; H, 6·1. $C_{18}H_{16}O_2$ requires C, 81·8; H, 6·1%). The *quinoxaline* separated from alcohol–chloroform in clusters of rods, m. p. 154—154·5° (Found: C, 85·8; H, 6·1; N, 8·3. $C_{24}H_{20}O_2$ requires C, 85·7; H, 5·9; N, 8·3%).

Oxidation of the Hydrocarbon $C_{18}H_{18}$.—The hydrocarbon (2·5 g.) was stirred at 90° with a

solution of potassium ferricyanide (500 g.) and potassium hydroxide (38 g.) in water (1·25 l.). After 30 and 60 hours, further amounts of oxidising agent (200 g. and 100 g.) and alkali (35 g. and 18 g.) were added and the reaction was continued for another 20 hours. The cold liquid was filtered, and the salts extracted with ether to recover unchanged hydrocarbon (0·6 g.). The aqueous solution was acidified with dilute sulphuric acid and extracted with ether for 48 hours. The ethereal solution was extracted with dilute alkali and the brown amorphous precipitate (0·2 g.; m. p. 140—150°) obtained on acidification was shaken with cold methyl alcohol. The soluble acid had m. p. 177—179° and the insoluble portion, m. p. 200—206°. These acids were dissolved in ether and esterified with diazomethane. The ester of the acid of higher m. p. solidified after 48 hours, but that from the acid, m. p. 177—179°, remained oily. The solid ester was fractionally crystallised from methyl alcohol. The first crop of crystals (1) consisted of small needles, m. p. 135—136°, and the second (2) of clustered needles, m. p. 135·5—136°, both of which were analysed [Found: (1) C, 74·2; H, 5·5; (2) C, 73·6; H, 5·0. $C_{18}H_{14}O_4$ requires C, 73·5; H, 4·7%].

We are greatly indebted to Messrs. A. Boake Roberts & Co. of Stratford, who kindly undertook the extraction of a large quantity of totara wood. Part of the cost of this investigation was defrayed by a grant from the Chemical Society.

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117. *The Tautomerism of Benzoquinoneoxime–*p*-Nitrosophenol Systems.*

By HERBERT H. HODGSON.

ALTHOUGH *p*-nitrosophenol and *p*-benzoquinoneoxime are prepared respectively by the action of nitrous acid on phenol and by the condensation of hydroxylamine with *p*-benzoquinone, yet the product in each case is represented by the tautomeric equilibrium $OH{\cdot}C_6H_4{\cdot}NO \rightleftharpoons O{:}C_6H_4{:}NOH$. From a spectroscopic study of this tautomerism, Baly, Edwards, and Stewart (J., 1906, **89**, 520) concluded that in neutral environment the nitroso-structure prevailed, whereas in alkaline solution the salt was in the quinoneoxime form. A like conclusion was reached by Hodgson and his collaborators (J., 1925, **127**, 2260; 1929, 1555; 1932, 1395) from the low melting point of *p*-nitrosophenol and its ability to react with diazomethane to give glyoxime *NN'*-di-4-methoxyphenyl ether. The diametrically opposite conclusion was drawn by Anderson and Geiger (*J. Amer. Chem. Soc.*, 1932, **54**, 3064), who argued that the absorption spectrum of each of the tautomerides, if it could be obtained pure, would be similar to that of its methyl ether, and since the methyl ethers do not undergo tautomerism under the conditions employed, a comparison of the spectra should aid the determination of the ratio of the tautomerides in the equilibrium mixture. The results of Anderson and Geiger were claimed to be confirmed by Anderson and Yanke (*ibid.*, 1934, **56**, 732) for the forms existing in the following solvents: ether, dioxan, chloroform, absolute alcohol, and aqueous acids; the experiments were also extended to measurements of the absorption spectra of 3-chloro-4-nitrosophenol, 3-chlorobenzoquinone-4-oxime, and their respective methyl ethers.

Anderson and Yanke (*loc. cit.*) found that the absorption spectrum of 3-chlorobenzoquinone-4-oxime was very similar to that of its methyl ether, but, most peculiarly, that of 3-chloro-4-nitrosophenol was unlike both that of its ether and that of its isomeric quinonoid modification. Since these authors could not ascribe such differences either to ionisation or to association of the nitrosophenolic form, for conductivity measurements indicated that the so-called tautomerides were dissociated to the same extent, they cited the work of Hantzsch (*Ber.*, 1917, **50**, 1422) on dissociable acids to resolve their dilemma, and stated that whatever the fundamental cause might be, it was probably explicable in the same terms for each group of compounds. Finally, Anderson and Yanke (*loc. cit.*) concluded that 2-chloro-4-nitrosophenol also existed mainly in the quinonoid modification because of the similarity between its absorption spectrum and that of 2-chlorobenzoquinone-4-

oxime methyl ether, notwithstanding the author's opposite conclusion (J., 1932, 866) based on incontrovertible chemical data.

The author and his collaborators have shown, and it has been confirmed by Anderson and Yanke, (i) that the 3-halogeno-4-nitrosophenols and the isomeric oximes are unimolecular in alcohol, benzene, chloroform, dioxan (pure and aqueous solutions), ether, naphthalene, phenol, and aqueous acids, and (ii) that, under all the experimental conditions as yet tried (including those of Anderson and his collaborators), the 3-halogenobenzoquinone-4-oximes could not be converted directly into the isomeric oximes, whereas the latter are rapidly transformed by alkalis into the former and more slowly by concentrated acids. In view of these facts, the conclusions of Anderson and his collaborators would appear to be premature and in some cases erroneous.

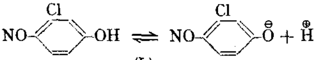
In order to support the chemical results by physical data, the absorption spectra of the 3-chloro-, 3-bromo-, and 3-iodo-4-nitrosophenols and of the corresponding isomeric oximes have now been measured in neutral, acid, and alkaline solutions. A similar study has also been made of 2-chloro-4-nitrosophenol, which, as judged by chemical data, exists only in the quinonoid modification in its salts and not in the free state. For comparison purposes, the absorption spectra of the methyl ethers of the above eight compounds have also been measured, together with those of *p*-nitrosophenol, *p*-nitrosoanisole, and *p*-benzoquinoneoxime methyl ether.

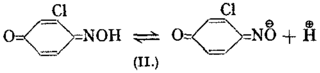
All the measurements now recorded were carried out with equivalent solutions of the several compounds in what was practically an aqueous medium, a condition which enabled ionisation (if any) to be freely developed, although Anderson and Yanke (*loc. cit.*), using dioxan–water mixtures as solvent, found that there was only a slight change in the absorption spectra during wide variations of the solvent composition. The resulting data are claimed to confirm the author's earlier conclusions based on purely chemical data, and also to resolve some of the difficulties abandoned by Anderson and his collaborators.

Apparatus.—The measurements were made with a polarisation type of spectrophotometer, the spectrograph being the Bellingham–Stanley Model No. 2, with quartz optical system of dispersion such that the spectrum from 2100 to 8000 A. was obtained on a single 10″ plate. The light source employed was the arc between iron electrodes in air. All the compounds were measured at the same molecular concentration in aqueous solutions containing but a trace of alcohol, and at a dilution of the order $4 \times 10^{-4}N$.

Discussion of the Absorption Spectra with Respect to the Chemical Constitution of the Compounds.

Since 3-chloro-4-nitrosophenol is a chemical individual which is obtained by the action of nitrous acid on *m*-chlorophenol (Hodgson and Moore, J., 1923, **123**, 2499) and crystallises unchanged from neutral solvents, including aqueous alcohol, with no evidence of its association, it is obvious that in neutral aqueous-alcoholic solution there should be present three entities, *viz.*, the un-ionised substance, its anion, and the hydrogen ion (I). The absorption spectrum (Fig. 1) confirms this anticipation, there being two very definite bands with peaks at 4010 and 2990 A.; these bands are eliminated respectively by excess of acid and of alkali (Fig. 2), and must therefore correspond respectively to the anion and the un-ionised 3-chloro-4-nitrosophenol. Similarly, 3-chlorobenzoquinone-4-oxime also must exist in neutral aqueous-alcoholic solution as an equilibrium between un-ionised substance and its ions (II), for the two absorption bands with peaks at 3030 and 3990 A. (Fig. 3) are eliminated respectively by excess of alkali and excess of acid (Fig. 4).


(I.)


(II.)

The apparent approximate identity of the above absorption spectra (compare Figs. 1 and 3) might lead to the premature conclusion that the substances were identical in solution, but such a deduction must be erroneous, since both substances separate unchanged

from aqueous alcohol, in which, incidentally, the quinoneoxime is far more soluble than the nitrosophenol. Furthermore, if tautomeric equilibrium were established on dissolution, then on subsequent crystallisation the solutions of both forms should afford the nitroso-form in the first separations, whereas the initial substance separates in a pure condition in each case. When, however, a mixture of 3-halogeno-4-nitrosophenol and the corresponding oxime is recrystallised from aqueous alcohol, it is the nitroso-form that

FIG. 1.

Absorption spectra of 3-halogeno-4-nitrosophenols in neutral solution.

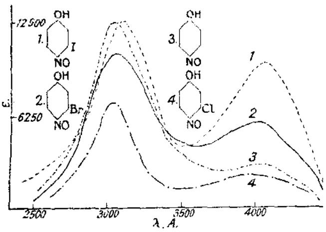
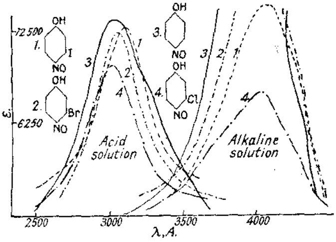


FIG. 2.

Absorption spectra of 3-halogeno-4-nitrosophenols in acid and alkaline solution.



separates first. Moreover, 3-chloro-4-nitrosophenol is exceedingly sensitive to reagents, and the 3-bromo- and the 3-iodo-analogue still more so, and all attempts to cause reaction with the phenolic hydrogen (Hodgson, *J.*, 1931, 1494) have resulted in conversion either into the quinoneoxime form itself or into that reaction product which the quinoneoxime affords under identical conditions. For example, both isomerides give the same silver salt, which on treatment with methyl iodide yields the 3-halogenobenzoquinone-4-oxime

FIG. 3.

Absorption spectra of 3-halogenobenzoquinone-4-oximes in neutral solution.

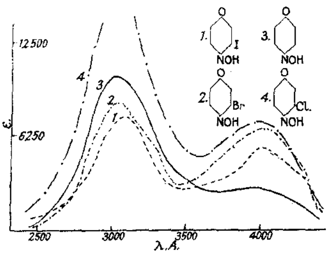
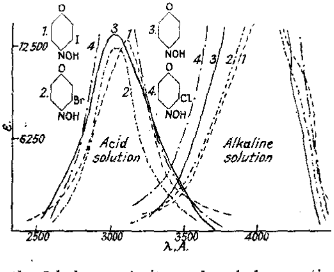


FIG. 4.

Absorption spectra of 3-halogenobenzoquinone-4-oximes in acid and alkaline solution.



methyl ether, a product also produced from the 3-halogeno-4-nitrosophenols by reaction with methyl sulphate and alkali and with ethereal diazomethane. Both isomerides (previously styled tautomerides) react with *p*-nitrophenylhydrazine to give the same *p*-nitrophenylhydrazone; further, dry hydrogen chloride rapidly converts the nitrosophenols into quinoneoximes in ethereal solution, and aluminium chloride and hydrogen chloride react vigorously with the 3-halogeno-4-nitrosoanisoles in dry ether to give the 3-halogenobenzoquinone-4-oximes. On the other hand, the 3-halogeno-4-nitrosophenols readily

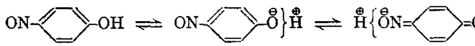
form unimolecular picrates, whereas the quinoneoximes do not, and diazomethane reacts with true nitroso-compounds to form derivatives of glyoxime, whereas quinoneoximes give rise to their methyl ethers.

Differences in the absorption spectra of these isomeric nitrosophenols and quinoneoximes should therefore be sought in the bands of the respective un-ionised compounds and of their anions identified as above, and such differences are found in the respective molecular extinction coefficients (ε), which vary markedly between the different compounds.

Anderson and Yanke (*loc. cit.*) found that the absorption spectra of their so-called quinoneoximes were very sensitive to changes in hydrogen-ion concentration between p_H 3 and p_H 7, and independent of these factors at p_H values outside this range. Such variations would naturally be expected, since changes of ionisation of the products in the weakly acid medium ($p_H > 3$) would be accompanied by pronounced changes in the densities of absorption, whereas in strongly acid medium ($p_H < 3$), the un-ionised product would alone exist and absorption would become constant so far as this product was concerned. Similarly, in an alkaline medium ($p_H > 7$), the un-ionised substance ceases to exist, and with complete ionisation the absorption becomes practically stabilised.

The two bands for 3-chloro-4-nitrosophenol have $\varepsilon = 6875$ and 1875 for 2990 A. and 4010 A. respectively, whereas the two bands of 3-chlorobenzoquinone-4-oxime have $\varepsilon =$ 15,000 for 3030 A. and $\varepsilon = 6875$ for 3990 A., indicating that very probably four distinct entities are being measured, *viz.*, the two un-ionised compounds and their respective ions; in presence of excess hydrochloric acid, which represses ionisation, the values of ε for the single bands of the un-ionised 3-chloro-4-nitrosophenol and of 3-chlorobenzoquinone-4-oxime become 8750 and 17,500 respectively, showing a small increase due to elimination of the ions. The ε's of the single bands of 3-chloro-4-nitrosoanisole and of 3-chlorobenzoquinone-4-oxime methyl ether are 10,625 for 3625 A. and 14,375 for 3180 A., and throughout the series the values of ε for the ethers are of the same order of magnitude as the values for the un-ionised hydroxylic compounds, the smaller ε's corresponding to the molecules under the greater electronic strain.

Similarly *p*-nitrosophenol itself exhibits two bands with peaks at 3020 and 3965 A. (Fig. 1), the former being suppressed by alkalis and the latter by acids (Fig. 2), and they therefore correspond to the un-ionised compound and an anion which perhaps in this case is in equilibrium with its tautomeric ion :



The chemical evidence, however, indicates that *p*-nitrosophenol in ethereal solution is mainly in the nitroso-form, since diazomethane converts it almost entirely into a glyoxime derivative (Hodgson, J., 1932, 1395), whilst the low m. p. of the solid, which is in the vicinity of the m. p.'s of the true 3-halogeno-4-nitrosophenols, points to the nitroso-structure in the crystalline state.

The above phenomena are repeated (see Figs. 1 and 3, and table) in the cases of 3-bromo- and 3-iodo-4-nitrosophenols and of the corresponding oximes. Whereas, however, the absorption curves for 3-chloro-4-nitrosophenol and its oxime form in acid and in alkaline solution indicate a considerable stability (retarded conversion for the nitroso-form), the corresponding curves for the bromo- and the iodo-analogue (Figs. 5 and 6) indicate that immediate conversion of both 3-bromo- and 3-iodo-4-nitrosophenol into the more stable quinoneoximes has taken place in both the acid and the alkaline environment. These facts support the chemical facts that 3-bromo- and 3-iodo-4-nitrosophenols are exceedingly sensitive to reagents and even to solvents (Hodgson and Moore, J., 1925, **127**, 2260).

The 3-halogeno-4-nitrosoanisoles (Fig. 7) exhibit very similar single absorption bands with their peaks at about 3625 A., *i.e.*, between the bands of the un-ionised and the ionic forms of the corresponding non-methylated compounds. The relative molecular extinction coefficients of these bands are of the same order, and all but one are less than that of the non-halogenated *p*-nitrosoanisole, which has its peak at 3500 A. and $\varepsilon = 13{,}750$. Any other minor peaks in the absorption spectra are probably due to the presence of un-

methylated compound arising from the incipient decomposition which sets in on keeping and results eventually in the complete conversion of the 3-halogeno-4-nitrosoanisole into the corresponding benzoquinone-4-oxime.

The methyl ethers of the 3-halogenobenzoquinone-4-oximes similarly possess single absorption bands (Fig. 8) with peaks at *ca.* 3200 A. and ε's *ca.* 12,000; *p*-benzoquinone-oxime methyl ether has its band very similarly situated to that of the 3-bromo-analogue.

FIG. 5.

Comparison of absorption spectra of 3-iodo-4-nitrosophenol and 3-iodobenzoquinone-4-oxime in neutral solution.

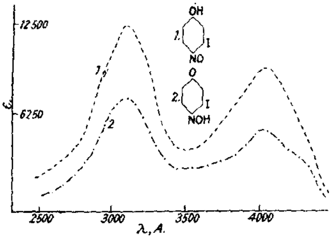
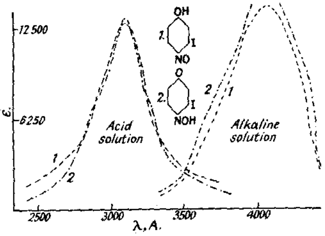


FIG. 6.

Comparison of the absorption spectra of 3-iodo-4-nitrosophenol and 3-iodobenzoquinone-4-oxime in acid and alkaline solution.



It will be obvious, therefore, that it may be highly fallacious to base conclusions as to the tautomeric form in which the substituted nitrosophenols and quinoneoximes exist on a mere comparison of their absorption bands with those of their respective methyl ethers. Further, Baker and Nathan (J., 1935, 1840) have pointed out that a special reaction mechanism must be assigned to the methyl group when attached to a conjugated system which differentiates it from the other alkyl groups, and the present author suggests

FIG. 7.

Absorption spectra of 3-halogeno-4-nitrosoanisoles.

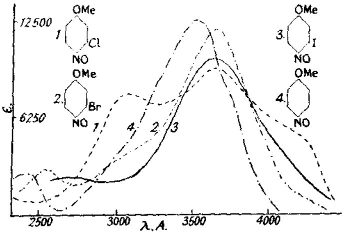
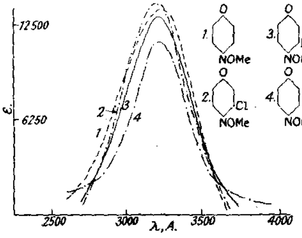


FIG. 8.

Absorption spectra of the 3-halogenobenzoquinone-4-oxime methyl ethers.



that such a possible rôle in other states of combination may vitiate any conclusions such as those which Anderson and his collaborators have drawn (cf. Ingold, *Chem. and Ind.*, **1936, 963**). Likewise, on Anderson's argument, the bands of the methyl ethers on such a comparison basis should correspond with those ascribed to the un-ionised compounds, and the accompanying table should completely reveal such a fallacy.

It will be noticed that the peak for nitrosobenzene itself occurs in the vicinity of those for the un-ionised compounds, thereby indicating that the nitroso- and the oximino-group are the prime centres of activity so far as absorption is concerned; that its wave-

TABLE.

(The molecular extinction coefficients, ε, corresponding to the various peaks are the mean values over all the measurements made.)

Compound.	Band due to ion. Peak (A.).	ε.	Band due to un-ionised compound. Peak (A.).	ε.	Band of methyl ether. Peak (A.).	ε.
3-Chloro-4-nitrosophenol	4010	1875	2990	6,875	3625	10,625
3-Bromo-4-nitrosophenol	4015	5625	3040	12,500	3620	11,875
3-Iodo-4-nitrosophenol	4050	9375	3080	12,500	3625	10,940
3-Chlorobenzoquinone-4-oxime	3990	6875	3030	15,000	3180	14,375
3-Bromobenzoquinone-4-oxime	4015	6250	3040	8,750	3200	13,125
3-Iodobenzoquinone-4-oxime	4030	5625	3080	7,500	3200	11,250
p-Nitrosophenol ⇅ *p*-Benzoquinoneoxime	3965	2500	3020	9,375	3500 (*p*-Nitrosophenol); 3280 (*p*-Benzoquinoneoxime)	13,750; 13,750
Nitrosobenzene	—		3160	—	—	—

length exceeds that of any un-ionised hydroxyl compound shows the greatest relief from electronic strain in the unsubstituted compound.

FIG. 9.

Absorption spectra of 2-chloro-4-nitrosophenol in neutral and acid solution.

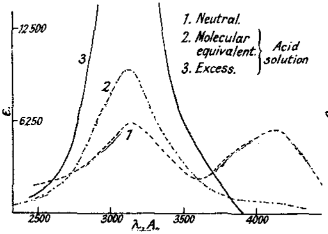
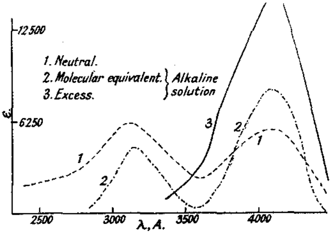


FIG. 10.

Absorption spectra of 2-chloro-4-nitrosophenol in neutral and alkaline solution.



Although Anderson and Yanke's experimental results are apparently confirmed in so far as the peaks of the bands of the quinone methyl ethers are nearer to those of the un-ionised compounds than are the corresponding peaks of the nitrosoanisoles, yet there is not even approximate identity between the bands themselves, and the differences can hardly be ascribed to the mere replacement of hydrogen by the methyl group, the system being far too complex for the toleration of such a conclusion. It will be noticed, however, that the bands of the methyl ethers have peaks in all cases at longer wave-lengths than those of the un-ionised compounds, whether of nitrosophenols or of quinoneoximes, and that this displacement conforms to the requirements of modern electronic theory, since the *inductive electron-repelling (+ I) effect of the methyl group is greater than that of* covalently bound hydrogen. On the other hand, the anions, in all cases, absorb at the longest wave-lengths, in conformity with the fact that they possess a free negative charge; since this charge must predominate over all other partial effects, the ionic absorption is found to be practically the same for most of the compounds.

The great disparity between the positions of the absorption bands for the un-ionised 3-halogeno-4-nitrosophenols and for the corresponding anisoles (of the order of 600 A.) can be accounted for by the much greater electronic strain in the phenols, resulting ultimately in ionisation, and, since the anticipated order of strain would be Cl > Br > I, this is confirmed by corresponding displacements of the bands both for the ionised and for the un-ionised parts of the dissociation equilibrium towards the longer wave-lengths in the order, Cl < Br < I, *i.e.*, corresponding to the order of strain. The 3-halogenobenzoquinone-4-oximes, on the other hand, are the more stable isomerides and incapable of

conversion into the nitroso-forms, so that the effects of groups are much less pronounced (the peak separation is of the order 150 A.) than in their much less stable nitroso-isomerides where the tendency (mesomeric) is towards conversion.

Anderson and Yanke (*loc. cit.*) dismiss the case of 2-chloro-4-nitrosophenol in one paragraph, in which they state that Hodgson concluded that the product existed in the benzenoid form from the simple fact of its low melting point. Anderson and Yanke ignore the other evidence which Hodgson accumulated in favour of his verdict, *viz.*, formation of a picrate, probable co-ordination between the chlorine atom and the hydroxyl group (cf. Sidgwick and Callow, J., 1924, **125**, 533), the recrystallisation of the compound unchanged from ether saturated with hydrogen chloride (cf. the facile transformation of the low-melting 3-chloro-isomeride into the much-higher-melting 3-chlorobenzoquinone-4-oxime), its precipitation unchanged from solutions in alkaline hydroxides and alkaline carbonates by mineral acids, and the significant facts that the quinoneoxime modification has only hitherto been found in its salts, in a methyl ether, and in condensation products with *p*-nitrophenylhydrazine and semicarbazide. Further, a subsequent publication by Hodgson (J., 1932, 1395) has been completely overlooked, in which diazomethane was reported as reacting with 2-chloro-4-nitrosophenol to form glyoxime *NN'*-di-3-chloro-4-methoxyphenyl ether and 2-chlorobenzoquinone-4-oxime methyl ether in approximately

FIG. 11.

Comparison of absorption spectra of 2-chloro- and 3-chloro-nitrosophenols in neutral solution.

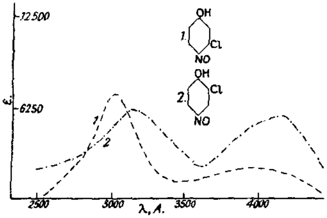
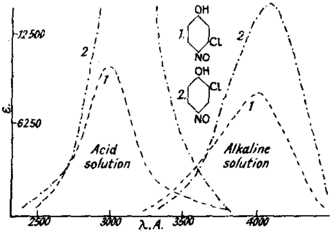


FIG. 12.

Comparison of absorption spectra of 2-chloro- and 3-chloro-4-nitrosophenols in acid and alkaline solution.



equal amounts. Now, diazomethane itself converts nitrosophenols into quinoneoximes and never effects the reverse process, so the quinoneoxime ether above is undoubtedly the result of partial isomerisation produced by the diazomethane, whereas sufficient retardation has been exerted by the tendency to chelation between hydroxyl and chlorine to favour the preservation of the nitroso-form in some molecules (about half the number) and their subsequent conversion into the glyoxime product.

The absorption spectrum of 2-chloro- is very similar to that of 3-chloro-4-nitrosophenol (Fig. 11) with two bands having peaks at 3125 A. ($\varepsilon = 6250$) and 4125 A. ($\varepsilon = 5625$) respectively, the band of longer wave-length being suppressed by acids and the other by alkalis (Fig. 10), and therefore corresponding to the anion and the un-ionised compound. Both bands are at longer wave-lengths than the corresponding pair of 3-chloro-4-nitrosophenol (2990 and 4010 A.), indicating that the electronic strain in the 2-chloro-compound is less than that in its 3-chloro-isomeride. The peak of the band given by 2-chloro-4-nitrosoanisole is at 3500 A., and that of 2-chlorobenzoquinone-4-oxime methyl ether at 3300 A. (Fig. 13), *i.e.*, nowhere near the peaks of 2-chloro-4-nitrosophenol itself (Figs. 9 and 10), so that, despite Anderson and Yanke's conclusion, based on their fallacious comparison of the ethers with the free phenol, it must be obvious that the product is in the benzenoid form. The low melting point rule of Hodgson and Moore (J., 1925, **127**, 2260), *viz.*, that "nitroso-compounds melt at a lower temperature than the isomeric quinoneoximes," is thus obeyed, and no exceptions to the rule have yet been recorded. It was the above

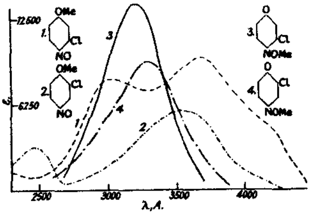
rule which led to a comprehensive investigation of 2-chloro-4-nitrosophenol, and the evidence was more detailed than is implied by Anderson and Yanke's simple statement (*loc. cit.*, p. 733) that "Hodgson . . . because of its low melting point, believes that it existed in the benzenoid form only."

It must also be pointed out that the data for *p*-nitrosophenol, *p*-nitrosoanisole, and *p*-benzoquinoneoxime methyl ether (see table and figures) are entirely in accord with the corresponding data for the substituted derivatives.

A trial, carried out in order to determine whether recrystallisation of 3-chloro-4-nitrosophenol from alcohol had any effect on the absorption spectrum, indicated no essential change, and thereby established conclusively that this substance retained its nitroso-structure after dissolution in hot alcohol.

FIG. 13.

Comparison of absorption spectra of 2-chloro- and 3-chloro-4-nitrosoanisoles and of 2-chloro- and 3-chloro-benzoquinone-4-oxime methyl ethers.



In the case of the measurements made in acid solution, separate data were obtained for hydrochloric and acetic acids, and both potassium hydroxide and sodium carbonate were used for the measurements in alkaline solution. This procedure provided a check, in addition to testing the possibility of different effects afforded by the highly and moderately ionised reagents. The fact that no appreciable variations were recorded, indicated that the ionisation was fully developed in each case owing to the extent of dilution required for the absorption measurements.

The author gratefully acknowledges his indebtedness to Dr. H. Lowery, Principal of the North-Western Polytechnic, London, for his interest and help extending over several years in connection with the above investigation, and to his research student, Mr. S. L. Harrison, M.Sc., Tech., for co-operation in the experimental section.

TECHNICAL COLLEGE, HUDDERSFIELD. [*Received, October 16th, 1936.*]

118. *The Polarity of the Co-ordinate Link. Part II. The Influence of Aromatic Substitution on the Stability of the Phosphinimines.*

By FREDERICK G. MANN and E. JAMES CHAPLIN.

IN Part I (Mann, J., 1932, 958) it was shown that there is a marked difference in the type of product obtained by the action of sodio-*N*-chloro-*p*-toluenesulphonamide ("chloramine-T"), $CH_3{\cdot}C_6H_4{\cdot}SO_2{\cdot}NNaCl,3H_2O$, on organic sulphides and on tertiary arsines. Sulphides react readily (often in cold aqueous suspension) with chloramine-T to give sulphilimines (I), whereas tertiary arsines give the corresponding hydroxy-sulphonamides (II). This difference was attributed to the fact that the co-ordinate link joining the

$$R_2S + NNaCl{\cdot}SO_2{\cdot}C_7H_7 = NaCl + R_2S{\rightarrow}N{\cdot}SO_2{\cdot}C_7H_7 \quad (I.)$$

$$R_3As + NNaCl{\cdot}SO_2{\cdot}C_7H_7 + H_2O = NaCl + AsR_3(OH){\cdot}NH{\cdot}SO_2{\cdot}C_7H_7 \quad (II.)$$

sulphur and the nitrogen atom in the sulphilimines is apparently devoid of polar properties, and such compounds are therefore stable even in the presence of water. The co-ordinate link joining the arsenic and the nitrogen atom in the arsinimines, $R_3As{\rightarrow}N{\cdot}SO_2{\cdot}C_7H_7$ (which are presumably the initial product in the above reaction) has, however, such strongly polar properties that the compound immediately combines with water to form the hydroxy-sulphonamide (II). This behaviour is parallel to that shown by most tertiary arsine oxides, $R_3As{\rightarrow}O$, where the co-ordinate link is so strongly polar that combination occurs freely, not only with acids such as nitric acid to give hydroxy-nitrates,

$AsR_3(OH)NO_3$ (a class of compound precisely similar to the hydroxy-sulphonamides), but also with water to give compounds such as $AsR_3(OH)_2$ and $AsR_3(OH){\cdot}O{\cdot}AsR_3(OH)$. The tertiary arsine hydroxy-sulphonamides were prepared also by the direct union of the corresponding arsine oxides and *p*-toluenesulphonamide, their constitution thus being proved.

The action of chloramine-T on tertiary phosphines has now been investigated, each phosphine, however, having been treated (*a*) with the anhydrous reagent in absolute-alcoholic solution, and (*b*) with the hydrated reagent in rectified spirit. It is clear, therefore, that under conditions (*a*) only a true phosphinimine, $R_3P{\rightarrow}N{\cdot}SO_2{\cdot}C_7H_7$, could be formed, whereas under (*b*) a phosphinimine or the hydroxyphosphine-sulphonamide (III), could be formed according to the strength of the polarity of the co-ordinate link in the initial phosphinimine.

(III.) $PR_3(OH){\cdot}NH{\cdot}SO_2{\cdot}C_7H_7$ $(C_7H_7{\cdot}SO_2{\cdot}NH{\cdot}PPh_3)_2N{\cdot}SO_2{\cdot}C_7H_7$ (IV.)

Triphenylphosphine under conditions (*a*) was found to give the true *phosphinimine*, $Ph_3P{\rightarrow}N{\cdot}SO_2{\cdot}C_7H_7$, whereas under (*b*) it gave NN-*bis*-(p-*toluenesulphonamidotriphenylphosphine*)-p-*toluenesulphonamide* (IV). The latter compound is identical in type with that given by triphenylarsine (Mann, *loc. cit.*), and it is noteworthy that no other phosphines or arsines were found to give this complex type of sulphonamide instead of the simple hydroxy-sulphonamide such as (III).

The effect of aromatic substituents in the triphenylphosphine molecule was then investigated, and the reaction of the *o*-, *m*-, and *p*-forms of tritolylphosphine, trianisylphosphine, $P(CH_3O{\cdot}C_6H_4)_3$, and trischlorophenylphosphine, $P(C_6H_4Cl)_3$, with chloramine-T under conditions (*a*) and (*b*) determined. The results are summarised in the table.

The Interaction of Tri-substituted Triphenylphosphines, $P(C_6H_4X)_3$, *with Chloramine-*T.

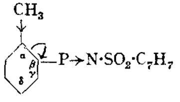
	Substituent, X.	(*a*) Anhydrous chloramine-T in absolute alcohol.	(*b*) Hydrated chloramine-T in rectified spirit.
Ortho-.	CH_3–	Phosphinimine	Phosphinimine
	CH_3O–	Phosphinimine	Phosphinimine + hydroxy-sulphonamide
	Cl–	Phosphinimine	Phosphinimine
Para-.	CH_3–	Phosphinimine	Phosphinimine + hydroxy-sulphonamide
	CH_3O–	Phosphinimine	Hydroxy-sulphonamide
	Cl–	Phosphinimine	Phosphine oxide + toluenesulphonamide
Meta-.	CH_3–	Syrup	Hydroxy-sulphonamide
	CH_3O–	Glass	Hydroxy-sulphonamide
	Cl–	*Amorphous solid*	*Phosphine oxide + toluenesulphonamide*

Tri-o-*tolylphosphine* thus gives a *phosphinimine* under both conditions (*a*) and (*b*), the presence of the three *o*-methyl groups suppressing the polarity of the P→N link and so inhibiting the formation of a hydroxy-sulphonamide; the same effect was found in the corresponding phosphine oxide, $(o\text{-}CH_3{\cdot}C_6H_4)_3P{\rightarrow}O$, in which the P→O link is too feebly polar to allow combination with *p*-toluenesulphonamide to give a hydroxy-sulphonamide. A similar but weaker effect was found with tri-*p*-tolylphosphine, which under conditions (*b*) gave a mixture of the *phosphinimine* and the *hydroxy-sulphonamide*: the polarity of the P→N link is evidently being less strongly suppressed by the three *p*-methyl groups, thus permitting some hydroxy-sulphonamide to be formed in the presence of water. Moreover, *p*-tolylphosphine oxide combined with *p*-toluenesulphonamide, but the hydroxy-sulphonamide so obtained dissociated again into its components in certain organic solvents. *Tri*-m-*tolylphosphine* under the anhydrous conditions (*a*) gave, however, only a thick viscous syrup. All attempts to isolate a crystalline derivative—either by the use of solvents, or by keeping the syrup under various conditions for many months—failed completely, and it is clear that a well-defined phosphinimine cannot be obtained. A very stable *hydroxy-sulphonamide* was, however, readily obtained when the *m*-tolylphosphine was treated with chloroamine-T under conditions (*b*), and also when the *phosphine oxide* was treated with *p*-toluenesulphonamide.

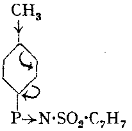
The effect of the methoxy-group in the trianisylphosphines, although similar through-

out to that of the methyl group in the tolylphosphines, was weaker, in that under conditions (*b*) the o-*methoxy-phosphine* gave a mixture of *phosphinimine* and *hydroxy-sulphonamide*, and the p-*methoxy-phosphine* gave solely the *hydroxy-sulphonamide*. The tris-chlorophenylphosphines also gave similar results with one marked exception, *viz.*, that the p- and the m-*chloro-phosphine* under conditions (*b*) did not give the expected hydroxy-sulphonamides but a mixture of the *phosphine oxide* and *p*-toluenesulphonamide.

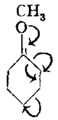
A complete theoretical interpretation of the above results is difficult. They are, however, clearly dependent on the fact that the three substituent groups studied (CH_3, CH_3O, and Cl) are all *op*-directing. Such groups cause an electron drift from themselves towards the benzene ring, either by the inductive effect of the substituent group followed by the resulting electromeric effect (V*a* and V*b*) or by the electromeric effect alone (VI and VII): in either case, an increase in the electrons on the β- and the δ-carbon atoms results. In the *o*-compounds, the cumulative effect of this electron pressure on the β-



(V*a*.)



(V*b*.)



(VI.)

(VII.)

carbon atoms of the three phenyl groups must be to decrease the dipole of the P→N group to which these atoms are directly attached (as in V*a*) and so to diminish the polarity of this group. In the *p*-compounds, the electron pressure on the δ-carbon atoms has the same result, but the effect is weaker owing to the greater distance involved (V*b*). The γ-carbon atoms are, however, almost unaffected by this electron drift, and hence in the *m*-compounds the P→N group exerts its full polarity: this is so great that apparently no well-defined phosphinimine exists, but a very stable hydroxy-sulphonamide is readily formed. In the chlorophenyl compounds (VII) the electromeric effect initiated by the chlorine atoms is, however, opposed by the inductive effect of these atoms, and this weakening may explain why in this series the phosphine oxides were obtained in place of the expected hydroxy-sulphonamides. On the other hand, contrary to the experimental results, the electromeric effect of the methoxy-group (VI) should have proved stronger than the inductive effect of the methyl group (V*a* and V*b*). The results are clearly unaffected by the *p*-toluenesulphonyl group, in view of the reaction of chloramine-T with sulphides and arsines under conditions (*b*).

This interpretation of the effect of the three *op*-directing groups would be strongly confirmed by similar experiments with derivatives of triphenylphosphine having *m*-directing substituent groups, for the above results should be reversed throughout, and only the *m*-substituted phosphine should readily give a stable phosphinimine. The Grignard reaction cannot be used for the preparation of such phosphines, however, and other synthetic methods have hitherto proved unsuccessful. Nevertheless, it is noteworthy that tri-*m*-nitrophenylphosphine oxide (Challenger and Wilkinson, J., 1924, **125**, 2675) will not combine with *p*-toluenesulphonamide: this is in accord with the above interpretation, since the *m*-nitro-groups should suppress the polar properties of the co-ordinate link in the phosphine oxide.

In view of the above results, the three tritolylarsines have now been treated with anhydrous chloramine-T under conditions (*a*), and precisely similar results obtained, the *o*- and *p*-tolylarsines giving true *arsinimines*, $(CH_3{\cdot}C_6H_4)_3As{\rightarrow}N{\cdot}SO_2{\cdot}C_7H_7$, whereas no well-defined product could be obtained from *m*-tolylarsine. The fact that all three tolylarsines give hydroxy-sulphonamides under conditions (*b*) (Mann, *loc. cit.*), whereas only the *p*- and the *m*-tolylphosphine do so, is evidently due to the As→N group having a greater polarity than the P→N group: this increase in polarity as the positive atom is

replaced by a heavier atom in the same periodic group is to be expected on other grounds (Sidgwick, " The Covalent Link in Chemistry" **1933**, p. 153).

The lower trialkylphosphines readily give phosphinimines under conditions (*a*); hydroxy-sulphonamides are apparently formed under conditions (*b*), but their low melting points and high solubility in most solvents make their isolation and purification difficult.

Since the phosphinimines are stereochemically analogous to the phosphine oxides (Meisenheimer and co-workers, *Ber.*, 1911, **44**, 356; *Annalen*, 1926, **449**, 213), attempts are now being made to prepare a suitable dissymmetric phosphinimine for optical resolution purposes.

EXPERIMENTAL.

The description of the preparation of each phosphine is followed by an account of its behaviour when under conditions (*a*) and (*b*) (see p. 528). The anhydrous chloramine-T was prepared by exposing the hydrated material to phosphoric oxide in a vacuum until the theoretical loss in weight was obtained. All derivatives, unless otherwise stated, were isolated as colourless crystals.

Triphenylphosphine was prepared by Dodonov and Medox's method (*Ber.*, 1928, **61**, 910). (*a*) Solutions of the phosphine (3 g.) and anhydrous chloramine-T (2·6 g., 1 mol.), each in hot absolute alcohol (40 c.c.), were mixed, sodium chloride rapidly separating. The mixture was boiled for 1 hour under reflux in a dry apparatus closed with a calcium chloride tube. The solution was then filtered, concentrated by direct distillation, and finally taken to dryness in a vacuum desiccator, crystals rapidly separating meanwhile. The complete dry residue, thrice recrystallised from benzene, gave *triphenylphosphine*-p-*toluenesulphonylimine*, m. p. 187° (Found : C, 70·2; H, 5·1; N, 3·2; S, 7·2. $C_{25}H_{22}O_2NSP$ requires C, 69·6; H, 5·1; N, 3·2; S, 7·4%). Consistent values for carbon were very difficult to obtain with all derivatives of triphenylphosphine, which thus differed from other phosphines studied, but resembled triphenylarsine (cf. Mann, *loc. cit.*; Davies, Pearse, and Jones, J., 1929, 1263). (*b*) A similar experiment, in which solutions of the phosphine (4 g.) and hydrated chloramine-T (4·4 g., 1 mol.) each in hot rectified spirit (50 c.c.) were used, gave on evaporation a syrup which rapidly solidified. Recrystallisation from benzene gave *NN-bis-(*p-*toluenesulphonamidotriphenylphosphine)*-p-*toluenesulphonamide* (IV), m. p. 138° (Found : H, 5·3; N, 4·1; S, 9·1; P, 5·7. $C_{57}H_{53}O_6N_3S_3P_2$ requires H, 5·2; N, 4·1; S, 9·3; P, 6·0%). The m. p.'s of this compound and of *p*-toluenesulphonamide are identical: that of a mixture is very much lower.

Triphenylphosphine oxide, m. p. 154° (Michaelis, *Annalen*, 1885, **229**, 305), was obtained by the addition of 1 mol. of bromine to the phosphine, followed by hydrolysis with hot sodium hydroxide solution; when benzene solutions of the oxide and of *p*-toluenesulphonamide (1·0 or 1·5 mols.) were boiled under reflux for 30 minutes and cooled, the above tris-sulphonamide was again obtained.

Tri-o-tolylphosphine was obtained by addition of a solution of phosphorus trichloride (6 g.) in ether (40 c.c.) to a Grignard reagent prepared by the action of magnesium (5·2 g.) upon *o*-bromotoluene (37 g.) dissolved in ether (100 c.c.); hydrogen was bubbled continuously through the well-stirred mixture during the addition. The final solution was then chilled, and the product hydrolysed with dilute hydrochloric acid. The ethereal layer was separated, dried over sodium sulphate, and the ether removed by distillation. The product was then heated to 280—290° under reduced pressure in a hydrogen atmosphere to remove by-products, and the residue when cold was crystallised from alcohol to give the phosphine, m. p. 125° (Found : C, 82·8; H, 7·1. $C_{21}H_{21}P$ requires C, 82·9; H, 7·0%).

(*a*) Solutions of the phosphine (10 g.) and anhydrous chloramine-T (7·5 g.), each in hot absolute alcohol (200 c.c.), were mixed and boiled under reflux for 2 hours. The solution was filtered, concentrated by distillation, and finally taken to dryness in a desiccator; recrystallisation of the solid from absolute alcohol gave *tri*-o-*tolylphosphine*-p-*toluenesulphonylimine*, m. p. 188° (Found : C, 71·1; H, 6·0; N, 3·0. $C_{28}H_{28}O_2NSP$ requires C, 71·0; H, 6·0; N, 3·0%). No other product could be isolated from the mother-liquors from the recrystallisation.

(*b*) A similar experiment, with 1 mol. of hydrated chloramine-T in rectified spirit, again gave the phosphinimine. The alcoholic mother-liquor from the first recrystallisation of the crude product was evaporated to dryness, and the residue, after recrystallisation from ethyl carbonate and then from alcohol, gave *tri-o-tolylphosphine oxide*, $P(C_7H_7)_3O,\frac{1}{2}H_2O$, m. p. 153° (Found : C, 76·7; H, 6·8. $C_{42}H_{44}O_3P_2$ requires C, 76·6; H, 6·7%), identical with that obtained by adding bromine to the phosphine and then boiling with aqueous sodium hydroxide for 12 hours to complete the hydrolysis. Since *p*-toluenesulphonamide was also isolated from

the mother-liquor, it is clear that the formation of the phosphinimine in rectified spirit is accompanied by that of some phosphine oxide and toluenesulphonamide, but that these do not combine to form a stable hydroxy-sulphonamide. This fact was confirmed by boiling an alcoholic solution of the oxide and the sulphonamide (1 mol.) for 30 minutes; evaporation of the solvent gave a solid residue from which the unchanged components were recovered by crystallisation.

Tri-*p*-tolylphosphine, m. p. 146°, was prepared as for the *o*-isomeride; Michaelis (*Annalen*, 1901, **315**, 79) prepared it by the action of sodium on a mixture of phosphorus trichloride and *p*-bromotoluene in ether.

(*a*) The phosphine was treated with anhydrous chloramine-T as described for the *o*-compound. Recrystallisation of the solid residue from alcohol gave *tri*-p-*tolylphosphine*-p-*toluenesulphonylimine*, m. p. 174° (Found: C, 71·1; H, 6·0; N, 2·9%).

(*b*) Reaction under these conditions, followed by evaporation, afforded a solid, which, recrystallised from alcohol, furnished the above phosphinimine. The alcoholic mother-liquor was evaporated to dryness, and the residue, recrystallised from ethyl carbonate, gave *hydroxytri*-p-*tolylphosphine*-p-*toluenesulphonamide*, m. p. 106° (Found: C, 68·4; H, 6·1; N, 2·8. $C_{28}H_{30}O_3NSP$ requires C, 68·4; H, 6·15; N, 2·85%). The same product was obtained by dissolving equimolecular quantities of the phosphine oxide, $P(C_7H_7)_3O,\frac{1}{2}H_2O$ (Michaelis, *loc. cit.*), and of *p*-toluenesulphonamide in hot alcohol, evaporating the solution to dryness, and recrystallising the residue from ethyl carbonate. The hydroxy-sulphonamide is unstable in solution, since a hot benzene solution of the pure compound on cooling deposited free *p*-toluenesulphonamide; no evidence that it would undergo dehydration to the phosphinimine could be obtained, however, a sample being unchanged after 8 months' exposure to phosphoric oxide in a vacuum.

Tri-m-*tolylphosphine*, prepared as for the *o*-isomeride, and recrystallised from alcohol, had m. p. 100° (Found: C, 82·6; H, 6·8%).

(*a*) The phosphine was treated with anhydrous chloramine-T as before, and evaporation of the solution gave a thick viscous syrup, which did not solidify when kept in a desiccator for a year; all attempts at recrystallisation from numerous solvents proved unsuccessful, the substance either remaining in solution or separating again as an intractable syrup. On one occasion a sample of the syrup was repeatedly washed with petrol (b. p. 60—80°) in which it was almost insoluble, and was then exposed to the air for 3 days, solidification slowly occurring; the product could be recrystallised only from ethyl carbonate, which deposited *hydroxytri*-m-*tolylphosphine*-p-*toluenesulphonamide*, m. p. 98° (Found: C, 68·3; H, 6·1; N, 3·0%).

(*b*) The product obtained under these conditions solidified immediately the alcohol was evaporated. Recrystallisation from either ethyl carbonate or alcohol readily furnished the hydroxy-sulphonamide (Found: C, 68·4; H, 6·2%), the m. p. being unchanged on admixture with the sample obtained as in (*a*); no other product could be detected.

Tri-m-*tolylphosphine oxide*, prepared by the addition of bromine to the phosphine, followed by hydrolysis and final recrystallisation from petrol (b. p. 100—120°), had m. p. 111° (Found: C, 78·7; H, 6·6. $C_{21}H_{21}OP$ requires C, 78·75; H, 6·6%). It is noteworthy that the phosphine dibromide was completely hydrolysed by 2 hours' boiling with aqueous sodium hydroxide solution, in contrast to the 12 hours required for the *o*-compound. Equimolecular quantities of the oxide and of *p*-toluenesulphonamide in hot alcoholic solution rapidly combined to give the above hydroxy-sulphonamide.

Tri-o-*anisylphosphine*.—*o*-Bromoanisole, prepared by the method of Diels and Bunzl (*Ber.*, 1905, **38**, 1496), was converted into a Grignard reagent and then treated with phosphorus trichloride, the same proportions of reagents and solvent being used as in the preparation of triphenylphosphine. The final chilled solution was now, however, hydrolysed with excess of an aqueous solution of ammonium chloride. The *phosphine*, being almost insoluble in cold ether, separated out during the hydrolysis, and was collected, dried, and recrystallised from much alcohol; it had m. p. 204° (Found: C, 71·4; H, 6·1. $C_{21}H_{21}O_3P$ requires C, 71·6; H, 6·0%).

(*a*) Solutions of the phosphine (3·0 g.) and anhydrous chloramine-T (2·0 g.) in hot absolute alcohol (200 and 50 c.c. respectively) were mixed and boiled for 2 hours. The solution was then treated as before, and the solid residue, recrystallised from a large volume of alcohol, gave *tri*-o-*anisylphosphine*-p-*toluenesulphonylimine*, m. p. 273—274° (Found: C, 64·6; H, 5·5; N, 2·7. $C_{28}H_{28}O_5NSP$ requires C, 64·45; H, 5·4; N, 2·7%).

(*b*) The solution resulting from the reaction of this type was finally evaporated to half bulk. On cooling, a large crop of the phosphinimine crystallised out; this was removed, and

the filtrate evaporated to dryness. The residue was extracted with hot benzene, and the solution, filtered from undissolved phosphinimine, deposited *hydroxytri-o-anisylphosphine-*p-*toluenesulphonamide*, which when recrystallised from benzene had m. p. 149° (Found: C, 62·2; H, 5·6; N, 2·7. $C_{28}H_{30}O_6NSP$ requires C, 62·3; H, 5·6; N, 2·6%).

The preparation of the phosphine oxide was attempted by the usual method of bromination followed by alkaline hydrolysis; the product, recrystallised from aqueous alcohol, proved to be *tribromotri-o-anisylphosphine oxide*, m. p. 245° (Found: C, 41·95; H, 3·1; Br, 39·3. $C_{21}H_{18}O_3Br_3P$ requires C, 41·7; H, 3·0; Br, 39·6%). The method of preparation shows that the bromine atoms are in the benzene ring and not in the methoxyl group; it is probable that the *m*-directing influence of the phosphorus atom reinforces the *o*-directing influence of the methoxyl group, and the groups P, OMe, and Br are in the 1, 2, and 3 positions respectively.

*Tri-*p-*anisylphosphine* was similarly prepared from *p*-bromoanisole, but after hydrolysis a portion of the phosphine had separated from the ether, whilst the rest remained dissolved in the ether and was recovered; recrystallisation from alcohol gave the pure phosphine, m. p. 131° (Found: C, 71·7; H, 6·0%).

(*a*) The phosphine was treated as before with anhydrous chloramine-T in absolute alcohol, and the residue, recrystallised from alcohol, gave *tri-*p-*anisylphosphine-*p-*toluenesulphonylimine*, m. p. 155° (Found: C, 64·4; H, 5·2; N, 2·6%).

(*b*) In order to determine whether the crude product obtained under conditions (*b*) was homogeneous, one portion was recrystallised from benzene, another from ethyl carbonate, and the remainder from carbon tetrachloride. Each solvent, however, furnished solely the *hydroxytri-*p-*anisylphosphine-*p-*toluenesulphonamide*, m. p. 121° (Found: C, 62·1; H, 5·6; N, 2·6%). No phosphinimine could be detected.

*Tri-*m-*anisylphosphine* was prepared similarly to the *p*-isomeride, part of the crude phosphine again separating from the ether and the remainder being recovered from the ethereal solution. Recrystallisation from alcohol gave the pure phosphine, m. p. 115° (Found: C, 71·4; H, 5·9%).

(*a*) Solutions of the phosphine (4 g.) and anhydrous chloramine-T (2·6 g.) in hot absolute alcohol (100 c.c. and 30 c.c. respectively) were mixed, the heat of the reaction causing the solvent to boil. The mixture was treated as before, but the final residue formed a thick viscous syrup; this, when kept for several days in a vacuum, solidified to a brittle glass, but neither the syrup nor the glass could be purified by recrystallisation. When the syrup was stirred with water, it was rapidly converted into the hydroxy-sulphonamide described below; if even traces of water were present in the initial reaction mixture, this was again obtained.

(*b*) Similar experiments but of this type gave a final residue, which rapidly solidified and when recrystallised from benzene afforded *hydroxytri-*m-*anisylphosphine-*p-*toluenesulphonamide*, m. p. 112° (Found: C, 62·1; H, 5·55; N, 2·7%). This compound is unstable in alcoholic or carbon tetrachloride solution, and recrystallisation from these solvents furnished *tri-*m-*anisylphosphine oxide*, m. p. 151—152° (Found: C, 68·2; H, 5·6. $C_{21}H_{21}O_4P$ requires C, 68·5; H, 5·7%). When, however, equimolecular quantities of the oxide and of *p*-toluenesulphonamide were dissolved in hot benzene, the pure hydroxy-sulphonamide again separated on cooling.

The Trischlorophenylphosphines.—These three phosphines were prepared by the action of phosphorus trichloride or tribromide on a Grignard reagent prepared from the corresponding chloroiodobenzene. The first experiments, however, furnished solely the corresponding phosphine oxides, owing to the fact that oxidation occurs very readily during the preparation, although the tertiary phosphines when isolated and purified are not readily oxidised. The difficulty was finally overcome by carrying out the entire preparation and subsequent hydrolysis in an atmosphere of hydrogen as before, and then blowing the reaction mixture by means of the compressed hydrogen directly from the apparatus through a delivery tube into a separating-funnel filled with carbon dioxide. When the aqueous layer had been removed, the ethereal solution was run into a conical flask containing sodium sulphate and previously filled with carbon dioxide; two delivery tubes (similar to those of a wash-bottle) were then fitted to the flask and closed. A small Buchner funnel, having a sintered-glass filter-plate, was fitted into the main neck of a suitable Claisen distilling-flask, and the funnel closed by a cork pierced by a delivery tube joined to the outlet tube of the conical flask. The dried ethereal solution was then slowly blown by compressed carbon dioxide over into the funnel, and the clear filtrate thus transferred to the distilling-flask without exposure to the air. The ether was distilled off, and the residue heated to 260° under reduced pressure in an atmosphere of hydrogen to remove by-products. The final residue was chilled whilst still exposed to hydrogen, and was then extracted with a minimum of hot alcohol, an insoluble viscous syrup remaining. In the case of all three chlorophenylphosphines, crystallisation occurred very slowly from the first alcoholic

extract, and was sometimes delayed for several days; subsequent recrystallisations occurred with increasing rapidity as the product became purer.

Tri-o-chlorophenylphosphine.—Concentrated hydrochloric acid (400 c.c.) was added in small quantities (*ca.* 20 c.c.) at a time to a mixture of *o*-chloronitrobenzene (126 g.) and granular tin (180 g.) contained in a large flask fitted with a reflux condenser. The mixture was occasionally shaken until the addition was complete, and was then heated on a water-bath for 2 hours, and finally made alkaline and steam-distilled. The *o*-chloroaniline was extracted with ether and obtained as an oil, b. p. 98—100°/20 mm. If an excess of hydrochloric acid is added during the reduction, the main product is 2 : 4-dichloroaniline (cf. Blanksma, *Rec. trav. chim.*, 1906, **25**, 368).

o-Chloroaniline (200 g.) was dissolved in a mixture of water (1200 c.c.) and concentrated hydrochloric acid (270 c.c.) at 70°. A further 270 c.c. of acid were then added, and the solution vigorously stirred whilst being chilled to − 5° to precipitate fine crystals of the hydrochloride. Sodium nitrite (110 g.) in water (250 c.c.) was then added, and the diazo-solution added in turn to potassium iodide (400 g.) dissolved in water (400 c.c.), a vigorous reaction ensuing. The mixture was then heated on a water-bath for 2 hours. The dark heavy oil was separated, added to 33% sodium hydroxide solution (200 c.c.), and steam-distilled. The *o*-chloroiodobenzene had b. p. 226—228°. Klages and Liecke (*J. pr. Chem.*, 1900, **61**, 321) gave b. p. 234—235°.

The phosphine was then prepared by the action of a solution of phosphorus trichloride (12·8 g.) in ether (50 c.c.) on a Grignard reagent prepared from magnesium (10·2 g.) and *o*-chloroiodobenzene (100 g.) in ether (200 c.c.). The chilled product was hydrolysed with a solution of ammonium chloride (50 g.) in water (250 c.c.), and finally worked up as described above. The *tri-o-chlorophenylphosphine*, when recrystallised from absolute alcohol, had m. p. 185° (Found : C, 58·9; H, 3·3; Cl, 29·2. $C_{18}H_{12}Cl_3P$ requires C, 59·1; H, 3·3; Cl, 29·1%); the yield was always low.

(*a*) Solutions of the phosphine (1 g.) and anhydrous chloramine-T (0·65 g.) in hot absolute alcohol (50 and 20 c.c. respectively) were mixed and then treated as before. Crystals separated whilst the final solution was evaporating in the desiccator. The oily residue, when recrystallised from alcohol, gave *tri-o-chlorophenylphosphine-p-toluenesulphonylimine*, m. p. 235—236° (Found : C, 56·0; H, 3·85; N, 2·7; Cl, 20·0. $C_{25}H_{19}O_2NCl_3SP$ requires C, 56·1; H, 3·6; N, 2·6; Cl, 19·9%).

(*b*) A similar experiment with hydrated chloramine-T in rectified spirit again gave the phosphinimine, no other product being detected.

Tri-o-chlorophenylphosphine oxide, $P(C_6H_4Cl)_3O,\frac{1}{2}H_2O$, was prepared by the usual method of bromine addition followed by hydrolysis, and also as a by-product in the first attempted preparations of the phosphine. Recrystallised from glycol monoethyl ether, the oxide formed beautiful leaflets, m. p. 226—236° (Found : H, 3·5; Cl, 27·3. $C_{18}H_{12}OCl_3P,\frac{1}{2}H_2O$ requires H, 3·4; Cl, 27·3%. Consistent values for carbon could not be obtained by micro- or macro-analysis).

All attempts made to unite the oxide and *p*-toluenesulphonamide in various solvents failed, the components being recovered unchanged.

Tri-p-chlorophenylphosphine.—The reduction of *p*-chloronitroaniline, unlike that of the *o*-compound, is not affected by an excess of acid. The nitro-compound (150 g.) was therefore dissolved in a hot mixture of water (450 c.c.), alcohol (800 c.c.), and concentrated hydrochloric acid (1100 c.c.) contained in a 5-litre flask fitted with a reflux condenser. Granular tin (180 g.) was added over a period of 1 hour, and the solution then boiled for at least 5 hours. Steam-distillation removed the alcohol, and then, when the solution was made alkaline, the *p*-chloroaniline, which was purified by recrystallisation from aqueous alcohol.

A solution of *p*-chloroaniline (100 g.) in a warm mixture of water (300 c.c.) and concentrated hydrochloric acid (300 c.c.) was cooled to 10° and diazotised with sodium nitrite (56 g.) in water (120 c.c.). The diazo-solution was added to potassium iodide (200 g. in 400 c.c. of water) as before, and the *p*-chloroiodobenzene isolated by steam-distillation. It was purified by distillation; m. p. 56°, b. p. 102—103°/12 mm.

Tri-p-chlorophenylphosphine, prepared as for the *o*-isomeride, had m. p. 103° after recrystallisation from absolute alcohol (Found : C, 59·4; H, 3·3; Cl, 29·0%).

(*a*) The phosphine, when treated as usual under these conditions, gave a product which rapidly crystallised during the evaporation. Recrystallisation of the crude dry product from much absolute alcohol gave *tri-p-chlorophenylphosphine-p-toluenesulphonylimine*, m. p. 232° (Found : C, 56·3; H, 3·8; N, 2·7; Cl, 19·9%).

(*b*) When the phosphine in rectified spirit was boiled with hydrated chloramine-T, and the

solution then slowly evaporated to dryness, crystals of m. p. 115—116° were obtained. These may have been a very unstable hydroxy-sulphonamide. When they were repeatedly recrystallised from benzene containing about 10% of *cyclo*hexane, pure *p*-toluenesulphonamide, m. p. and mixed m. p. 137—138°, was obtained; the filtrate from the first recrystallisation, when evaporated to dryness and recrystallised from ethyl carbonate, gave *tri*-p-*chlorophenylphosphine oxide*, m. p. 175° (Found: Cl, 27·7. $C_{18}H_{12}OCl_3P$ requires Cl, 27·9%). When an alcoholic solution of the oxide and of *p*-toluenesulphonamide was boiled, no combination could be detected; a portion of the residue obtained by complete evaporation gave the oxide on recrystallisation from ethyl carbonate, and the remainder gave the unchanged sulphonamide from benzene. It is noteworthy that the phosphinimine was also obtained when the phosphine was treated with *hydrated* chloramine-T in absolute alcohol; its formation is therefore not inhibited by *small* quantities of water.

Tri-m-*chlorophenylphosphine*.—*m*-Chloroaniline, *m*-chloroiodobenzene, and this *phosphine* were prepared similarly to the *o*-isomerides. The last compound, when recrystallised from alcohol, had m. p. 67° (Found: C, 59·1; H, 3·3; Cl, 28·9%). The yield of the *p*- and the *m*-chloro-phosphine was always considerably higher than that of the *o*-compound.

(*a*) The phosphine, by the usual procedure, gave finally a white solid residue. The only suitable solvent found for purification was rectified spirit, from which the residue on repeated recrystallisation gave tri-*m*-chlorophenylphosphine oxide, m. p. 135° (Found: Cl, 27·5. Calc. for $C_{18}H_{12}OCl_3P$: Cl, 27·9%). Challenger and Wilkinson (*loc. cit.*) gave the same m. p.

(*b*) Under these conditions, the phosphine furnished a solid residue which, when recrystallised from either alcohol or ethyl carbonate, gave only the above oxide.

A solution of tri-*m*-nitrophenylphosphine oxide (1 g.) and *p*-toluenesulphonamide (0·42 g.) in acetone (150 c.c.) was boiled under reflux for 30 minutes and then evaporated to 50 c.c.; on cooling, the unchanged phosphine oxide crystallised out. Similar solutions were prepared in dioxan (30 c.c.) and also in glycol monoethyl ether (35 c.c.) and boiled as before; on cooling (without concentration) the unchanged oxide separated in each case.

Phenyldimethylphosphine.—A mixture of benzene (275 g.), phosphorus trichloride (400 g.), and aluminium chloride (60 g.) was boiled under reflux for 50 hours; the whole of the liquid product was then distilled off and finally fractionated under reduced pressure, the resulting phenyldichlorophosphine having b. p. 105—107°/23 mm. Phenyldimethylphosphine was then prepared by the action of the dichloro-phosphine (25 g.) in ether (50 c.c.) on a Grignard reagent prepared from magnesium (12·1 g.) and methyl iodide (71 g.) in ether (150 c.c.); it had b. p. 82°/20 mm. Meisenheimer (*Annalen*, 1926, **449**, 227) gives b. p. 83—84°/13·5 mm.

(*a*) Solutions of the freshly distilled phosphine (2 g.) and anhydrous chloramine-T (3·3 g.), each in hot absolute alcohol (20 c.c.), were mixed, the usual precipitation of sodium chloride immediately occurring. Evaporation finally gave a mobile oil, which refused to solidify, and from which no crystalline product could be obtained.

(*b*) These conditions also afforded a mobile oil, which dissolved readily in cold benzene, and did not therefore contain free *p*-toluenesulphonamide. Since, however, the oil could not be directly recrystallised, it was extracted with a hot mixture of carbon tetrachloride and benzene. The solution deposited an oil, which solidified after several days. It was then recrystallised from benzene–*cyclo*hexane, and *p*-toluenesulphonamide, m. p. 137—138°, was ultimately obtained. The mother-liquors undoubtedly contained the very soluble phenyldimethylphosphine oxide.

Phenyldiethylphosphine.—Prepared as for the dimethyl compound, but from ethyl iodide (78 g.), the phosphine had b. p. 108—109°/20 mm. Meisenheimer (*loc. cit.*) gives b. p. 96—98°/10 mm. The phosphine, when treated with chloramine-T under either conditions (*a*) or (*b*), gave *phenyldiethylphosphine*-p-*toluenesulphonylimine*, m. p. 82° after recrystallisation from alcohol (Found: C, 61·2; H, 6·6; N, 4·2. $C_{17}H_{22}O_2NSP$ requires C, 60·9; H, 6·6; N, 4·2%).

By similar methods were prepared *p*-tolyldichlorophosphine (Michaelis and Paneck, *Annalen*, 1882, **212**, 206) [toluene (300 g.), phosphorus trichloride (400 g.), aluminium chloride (60 g.)], b. p. 122—125°/21 mm., and *p*-tolyldimethylphosphine, b. p. 93—95°/12 mm. This phosphine, when treated with chloramine-T under conditions (*a*) and (*b*), gave results similar to those of the phenyl compound, no phosphinimine or stable hydroxy-sulphonamide being isolated.

p-Tolyldiethylphosphine, prepared similarly to the phenyl compound, had b. p. 114—115°/12 mm. Treatment of the freshly distilled phosphine with chloramine-T under conditions (*a*) or (*b*) gave p-*tolyldiethylphosphine*-p-*toluenesulphonylimine*, m. p. 120° after recrystallisation from alcohol (Found: C, 62·3; H, 6·9; N, 4·0. $C_{18}H_{24}O_2NSP$ requires C, 61·9; H, 6·9; N, 4·0%).

It is probable from these results that a methyl group attached to the phosphorus atom inhibits hydroxy-sulphonamide formation: similar results were obtained with the arsines (Mann, *loc. cit.*).

The following *trialkylphosphine*-p-*toluenesulphonylimines* were prepared by method (*a*): evaporation in a desiccator gave a mobile oil which usually did not solidify until it was exposed to the air and scratched with a rod: *triethyl* compound, m. p. 119° from alcohol (Found: C, 54·6; H, 7·5; N, 5·1. $C_{13}H_{22}O_2NSP$ requires C, 54·3; H, 7·7; N, 4·9%); *tri*-n-*propyl* compound, m. p. 66° from ether (Found: C, 58·1; H, 8·5; N, 4·2. $C_{16}H_{28}O_2NSP$ requires C, 58·3; H, 8·55; N, 4·25%); *tri*-n-*butyl* compound, m. p. 54° from *cyclo*hexane (Found: C, 61·8; H, 9·1; N, 3·9. $C_{19}H_{34}O_2NSP$ requires C, 61·4; H, 9·2; N, 3·8%). The solubilities of the alkyl compounds in the usual organic solvents increase rapidly as the homologous series is ascended. Treatment of the propyl- and the butyl-phosphine with hydrated chloramine-T gave semi-solid products from which no pure crystalline compound was isolated.

Triphenylarsine-p-*toluenesulphonylimine*.—Solutions of triphenylarsine (3 g.) and anhydrous chloramine-T (2·3 g.), each in absolute alcohol (30 c.c.), were mixed and treated as usual. The final residue rapidly solidified, and on recrystallisation from absolute alcohol gave the *arsinimine*, m. p. 192—193° (Found: H, 4·6; N, 3·0; S, 6·5. $C_{25}H_{22}O_2NSAs$ requires H, 4·65; N, 2·95; S, 6·7%. Consistent values for C could not be obtained).

The *tri*-o-*tolylarsine*-p-*toluenesulphonylimine*, similarly obtained from tri-*o*-tolylarsine (2·0 g.) and anhydrous chloramine-T (1·3 g.), each in 40 c.c. of absolute alcohol, and recrystallised from absolute alcohol, had m. p. 201—202° (Found: C, 65·2; H, 5·5; N, 2·8. $C_{28}H_{28}O_2NSAs$ requires C, 64·9; H, 5·45; N, 2·7%). The *tri*-p-*tolylarsinimine*, similarly obtained and recrystallised, had m. p. 185° (Found: C, 65·1; H, 5·6; N, 2·8%).

A similar experiment performed with tri-*m*-tolylarsine gave a viscous oil which did not solidify for several days, and then formed a waxy solid from which no crystalline derivative could be obtained.

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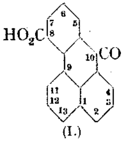
THE UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, January 25th*, 1937.]

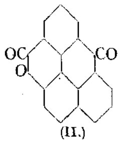
119. *Oxidation Products of Benzanthrone-8-carboxylic Acid.*

By JOHN L. GRIEVE and H. GORDON RULE.

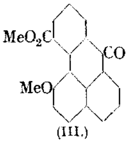
IN an earlier communication dealing with the action of hot concentrated sulphuric acid upon benzanthrone-8-carboxylic acid (I), a yellow compound was described which dissolves slowly in alkali to give a brilliant red solution having a vivid green fluorescence. This compound was also isolated in good yield by oxidising the acid with chromic acid and was tentatively formulated (II) as the lactone of 11-hydroxybenzanthrone-8-carboxylic acid (Bigelow and Rule, *J.*, 1935, 573), although it was not found possible to support this structure by the preparation of a methylated or decarboxylated derivative.



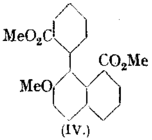
(I.)



(II.)



(III.)



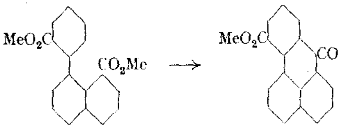
(IV.)

Confirmation of the lactone formula has now been obtained by a synthesis effected in the following stages: *methyl 8-bromo-7-methoxy-1-naphthoate* was condensed with methyl *o*-iodobenzoate in the presence of copper bronze to give an intermediate *phenylnaphthalene-dicarboxylate* (IV), which on brief treatment with warm concentrated sulphuric acid was converted quantitatively into a compound identical with the above oxidation product.

Benzanthrone itself is known to undergo oxidation in positions 2 and 12, but the entry

of oxygen into position 11 is a somewhat unexpected phenomenon. The reaction is not to be explained by the presence of the 8-carboxyl group, except possibly on the assumption that it is facilitated by the spatial disposition of this group with respect to the rest of the molecule, which is such that a new stable six-membered ring may be formed as a result of oxidation at position 11. Profound modifications in the normal properties of substituent groups undoubtedly occur in molecular structures of this kind where two or more groups of atoms are maintained rigidly in permanent proximity to one another, as is illustrated further by the novel behaviour of the intermediate esters (III) and (IV) towards hydrolysing agents.

Earlier work has shown that the dimethyl ester of 8-*o*-carboxyphenyl-1-naphthoic acid on treatment for 1 hour at 50° with concentrated sulphuric acid is converted into methyl benzanthrone-8-carboxylate, and that further heating at 100° is required to hydrolyse this ester to the free acid (Bigelow and Rule, *loc. cit.*). By analogy it was hoped

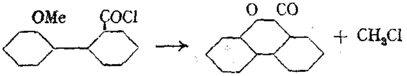


to effect a similar series of changes with the methoxy-ester (IV), leading to the isolation of the benzanthrone derivative (III) and its hydrolysis product, 11-methoxybenzanthrone-8-carboxylic acid. This last compound on decarboxylation might have been expected to yield the unknown 11-methoxybenzanthrone. In actual practice, however, the complete transformation could not be achieved, as treatment of (IV) for even a short time with sulphuric acid or other cyclising agent brought about direct conversion into the lactone.

A small yield of the desired *methyl 11-methoxybenzanthrone-8-carboxylate* was eventually isolated together with much lactone by warming the phenylnaphthalene derivative (IV) with an acetic acid solution of sulphuric acid. The product was a brilliantly yellow, crystalline solid which dissolved in the majority of organic solvents to form solutions with a vivid green fluorescence. Brief treatment with cold concentrated sulphuric acid sufficed to convert the ester into lactone. This reaction is the more surprising in view of the resistance to acid hydrolysis normally offered not only by a methoxyl group but also by the ester group of methyl benzanthrone-8-carboxylate, and the facile change appears to be due to the peculiar stereochemical relationship of the interacting groups.

Such a conclusion is supported by the behaviour of the methoxybenzanthronecarboxylic ester towards alkalis, five hours' heating with alcoholic potash converting it largely into the lactone. None of the intermediate 11-methoxybenzanthrone-8-carboxylic acid could be isolated, and this compound would appear to be unstable under the experimental conditions employed, despite the normal stability of a methoxyl group towards alkalis. These results, however, are in complete agreement with the failure of all attempts to methylate the lactone (Bigelow and Rule, *loc. cit.*). On the other hand, the uncyclised ester (IV), in which the phenyl group is able to rotate freely around the bond joining it to the naphthalene nucleus, may be hydrolysed in the usual way with alcoholic alkali to yield the corresponding stable *methoxy-dicarboxylic acid*. All reactions designed to effect a partial cyclisation of the latter to methoxybenzanthronecarboxylic acid again led solely to the production of lactone.

A somewhat analogous phenomenon to the above has previously been recorded in the case of 2-methoxydiphenyl-2'-carboxylic acid, the acid chloride of which passes spontaneously even at low temperatures into the lactone of the 2-hydroxy-acid, with elimination of methyl chloride (Rule and Bretscher, J., 1927, 925):



As the acid oxidation of benzanthrone-8-carboxylic acid gave no isolable product apart from the lactone, an examination was made of its reaction towards alkaline permanganate as employed by Allen and Overbaugh (*J. Amer. Chem. Soc.*, 1935, **57**, 740) and Charrier and Ghigi (*Ber.*, 1936, **69**, 2211). By use of this reagent a small amount of the hitherto unknown *anthraquinone-1 : 8-dicarboxylic acid* has now been isolated, the structure of which has been confirmed by sublimation in the presence of copper bronze to give anthraquinone.

EXPERIMENTAL.

8-Bromo-7-methoxy-1-naphthoic acid was prepared by the method of Davies, Heilbron, and Irving (J., 1932, 2715), but modified by use of alkaline hydrogen peroxide (Whiston, *J. Soc. Chem. Ind.*, 1924, **43**, 370) for converting the intermediate methoxyacenaphthenequinone into 2-methoxynaphthalic acid (yield, 92%). *Methyl* 8-*bromo*-7-*methoxy*-1-*naphthoate*, obtained by way of the acid chloride, crystallised from light petroleum in stout needles, m. p. 79° (Found : Br, 27·0. $C_{13}H_{11}O_3Br$ requires Br, 27·1%).

A mixture of the above ester (20 g.) with methyl *o*-iodobenzoate (40 g.) was heated with stirring to 150°. Copper bronze (25 g.) was then added during 1 hour, and the temperature maintained at 175° for 3 hours. The cooled product was extracted with acetone (150 c.c.), and after removal of the solvent under diminished pressure the syrupy residue was treated with ether (25 c.c.). The solid deposited, on recrystallisation from ligroin, gave colourless prisms (11·0 g.) of *methyl* 7-*methoxy*-8-(o-*carbomethoxyphenyl*)-1-*naphthoate*, m. p. 137° (Found : C, 71·9; H, 5·2. $C_{21}H_{18}O_5$ requires C, 72·0; H, 5·2%).

The above dimethyl ester was examined as follows : (*a*) 1·5 G., treated for 5 minutes at room temperature with concentrated sulphuric acid, gave a theoretical yield of the lactone of 11-hydroxybenzanthrone-8-carboxylic acid, m. p. 356°, unchanged on admixture with the product obtained by oxidising benzanthrone-8-carboxylic acid with chromic acid. (*b*) Mild fusion with zinc chloride, warming with thionyl chloride, or boiling with phosphoric oxide in nitrobenzene, again effected cyclisation to the lactone. (*c*) 0·5 G. in 10 c.c. of glacial acetic acid was treated with 2 c.c. of concentrated sulphuric acid and maintained at 80° for 15 minutes. On pouring into water, and boiling for 10 minutes with alkali to dissolve lactone, a small residue of *methyl* 11-*methoxybenzanthrone*-8-*carboxylate* remained. This crystallised from alcohol in brilliant yellow needles (0·06 g.; 13%), m. p. 194° (Found : C, 75·4; H, 4·4. $C_{20}H_{14}O_4$ requires C, 75·1; H, 4·5%). The ester (0·56 g.), on being boiled for 5 hours with potassium hydroxide (10 g.) in alcohol (50 c.c.), gave a solution from which only lactone (0·32 g.) and unchanged starting material (0·1 g.) could be isolated.

7-Methoxy-8-(o-carboxyphenyl)-1-naphthoic Acid.—The ester (IV) (1 g.) was boiled for 24 hours with alcoholic potassium hydroxide. Acidification gave a precipitate of 7-*methoxy*-8-(o-*carboxyphenyl*)-1-*naphthoic acid* (0·75 g.; 82%), which crystallised from alcohol in colourless rhombs containing alcohol of crystallisation. After being heated at 150° for 30 minutes, these melted at 239° (Found : C, 70·8; H, 4·4. $C_{19}H_{14}O_5$ requires C, 70·8; H, 4·4%). The acid dissolves in concentrated sulphuric acid to a red solution, being rapidly converted into the lactone. The cyclising agents mentioned above, including a dilute solution of sulphuric acid in acetic acid, also led to the formation of lactone, no other products being isolated.

Alkaline Oxidation of Benzanthrone-8-carboxylic Acid.—The acid (1 g.), sodium hydroxide (1 g.), and potassium permanganate (2 g.) were dissolved in water (150 c.c.), and the mixture boiled for 20 hours. Filtration, followed by acidification, threw out 0·2 g. of unchanged starting material; this was removed, and the clear liquid evaporated almost to dryness. A small yield of *anthraquinone*-1 : 8-*dicarboxylic acid* was obtained, readily soluble in hot water and in alcohol, crystallising from the latter solvent in light yellow octahedra (0·04 g.), m. p. 316—317° (decomp.) (Found : C, 65·0; H, 2·9. $C_{16}H_8O_6$ requires C, 64·9; H, 2·7%). When the acid (0·1 g.), mixed with a trace of copper bronze, was heated for 5 minutes at 320°, and the product sublimed under reduced pressure, neutral yellow needles of anthraquinone were obtained (0·06 g.; 85%), m. p. and mixed m. p. 285°.

Grateful acknowledgement is made to the Carnegie Trust for a Scholarship (to J. L. G.) and a Teaching Fellowship (to H. G. R.), and to Imperial Chemical Industries, Ltd., for a grant.

EDINBURGH UNIVERSITY. [*Received, February 17th, 1937.*]

120. *The Functional Relation between the Constants of the Arrhenius Equation.*

By R. A. Fairclough and C. N. Hinshelwood.

(1) *Introduction.*

In the reaction-velocity equation $k = PZe^{-E/RT}$ the constants PZ and E, instead of being independent, have sometimes been found to exhibit a correlation, PZ increasing with E through a series of reactions (see Moelwyn-Hughes, "Kinetics of Reactions in Solution," Oxford, 1933, p. 167). We have observed and studied some well-defined examples of this effect, where the changes in E and P caused by alteration of the medium show a close functional relation.

Fig. 1.

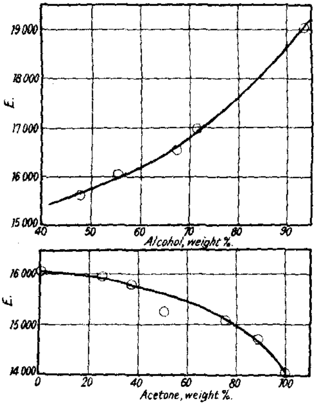
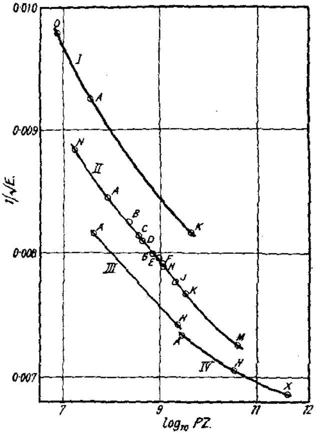


Fig. 2.



I, Alkaline hydrolysis of methyl acetate. II, Alkaline hydrolysis of ethyl benzoate. III, Formation of methylpyridinium iodide. IV, Hydrolysis of ethyl bromide.

In the first section of this paper we shall consider whether these relations can be more than accidental, and then, after a discussion of the experimental results, we shall consider an explanation, based upon general statistical principles (Section 4), which leads us to some general considerations about the function of the medium in chemical reactions, and the nature of the probability factor P.

The correlation of P and E would lose its significance if the data examined related only to reactions selected for study because they proceed at conveniently measurable rates in a given temperature interval. Even if any value of P could occur with any value of E, only those reactions would have been chosen for experiment in which the values of P and E so compensated one another as to give what was considered the convenient rate.

Since our plan has been to study the changes in the velocity of a given reaction caused by systematic variations in the medium, without reference to the convenience of the measurements, there is no question of such automatic selection of data.

There is also doubt about the reality of the correlations when data of unspecified

accuracy are used: log PZ is calculated by adding log k to E/RT; E is less accurately measurable than log k. If E has been overestimated then the value of log PZ will be correspondingly too large. In the experiments to be described, the possibility of plotting the values of E, as a function, not merely of PZ, but also of the composition of the medium, gives an independent control of their reliability (Fig. 1).

The starting point of the experiments was the observation that the values of E and PZ for the alkaline hydrolysis of ethyl benzoate were both considerably increased when the medium was changed from aqueous acetone to aqueous alcohol (Newling and Hinshelwood, J., 1936, 1357; Ingold and Nathan, J., 1936, 222).

Measurements were then made with a ternary system, the water concentration being kept constant, and the ratio of acetone to alcohol varied. The values of E changed regularly with composition (Fig. 1), and log PZ increased almost linearly with increasing E. The correlation may also be expressed as a decrease in log PZ with increase in $1/\sqrt{E}$ (Fig. 2), a form indicated by the theoretical treatment of Section 4.

Experiments were then made with alcohol–water mixtures of various proportions and a dioxan–water mixture. The functional relation of E and PZ persisted throughout.

Three other reactions, the alkaline hydrolysis of methyl acetate and of ethyl bromide, and the formation of methylpyridinium iodide, investigated in a similar range of media, showed analogous relationships (Fig. 2).

(2) *Experimental Details and Results.*

The solvents used were mixtures of water, acetone, alcohol, and dioxan in various proportions. Acetone was purified by fractionation with a five-foot Dufton column, alcohol by refluxing over freshly burnt lime for five hours and fractionating, and dioxan by repeated crystallisation from the melt. Ordinary distilled water was used, but was freed from carbon dioxide by boiling. Alcohol–water mixtures were prepared, and the percentage of alcohol by weight determined from density measurements. The alcohol–acetone–water mixtures A—F were prepared according to the following scheme: 400 g. of water were made up to one litre with a previously prepared mixture containing a given proportion by weight of acetone in alcohol. Thus the normality of the water was constant throughout this series. The dioxan–water mixture, N, also contained 400 g. of water in one litre of solvent. Some relevant properties of these solvents are given in Table I, $\varepsilon^{20°}$ being the dielectric constant at 20°, and the Jowett correction being $-RT^2 \,.\, d \log \eta/dT$ (see p. 541).

TABLE I.

Solvent, and composition. 400 G. of H_2O made up to 1 l. by acetone–alcohol containing w% of acetone by weight.	w.	$d_{4°}^{25°}$.	$\varepsilon^{20°}$.	Jowett correction.
A	100·0	0·903	46	—
B	88·95	0·902	—	4560
C	75·04	0·901	—	4765
D	50·50	0·901	—	5030
E	36·97	0·900	—	5430
F	25·04	0·898	—	5530
H	0·0	—	46	6220

Solvent, and composition. Alcohol–water mixtures: weight % of alcohol = w, mole-fraction = x.	w.	x.	$\varepsilon^{20°}$.	Jowett correction.
G	47·9	0·269	51	6520
H	55·7	0·334	46	6220
I	67·1	0·444	40	5650
K	71·3	0·493	38	5400
M	93·5	0·850	28	3850
N	Dioxan–water: 400 g. H_2O/l.	—	25	—
O	Water	—	81	—

All the reacting substances were purified by fractionation, and boiled over a narrow range at the correct temperatures. The pyridine had been dried over potassium hydroxide.

All activation energies were determined from measurements at four temperatures. The usual electrically controlled thermostats were used for temperatures other than 0°, where a Dewar vessel containing crushed ice and water was used. Thermometers were compared with N.P.L. standards. Glassware was standardised. All velocity constants were corrected for change of concentration due to thermal expansion of solvent.

Alkaline hydrolysis of ethyl benzoate. This was followed by the usual alkalimetric titration method, cresol-red being used as indicator. With solutions containing acetone, unusual care had to be taken to exclude carbon dioxide.

The concentrations of the mixed reactants were $N/20$. Satisfactory bimolecular constants were found, and the Arrhenius equation was followed.

The dioxan–water solution caused much difficulty; the bimolecular constants fell as the reaction proceeded, as though the solvent were undergoing a progressive change, which, as far as we could tell, was not due to absorption of carbon dioxide. To circumvent the difficulty, initial rates of reaction were taken.

The results are collected in Table II, and the value of log PZ is plotted against $1/\sqrt{E}$ in Fig. 2.

TABLE II.

*Hydrolysis of ethyl benzoate.**

Solvent A.		Solvent B.		Solvent C.		Solvent D.		Solvent E.		Solvent F.	
Temp.	$k \times 10^4$.	Temp.	$k \times 10^4$.	Temp.	$k \times 10^4$.	Temp.	$k \times 10^4$.	Temp.	$k \times 10^4$.	Temp.	$k \times 10^4$.
0·11°	4·05	−0·02°	3·19	0·45°	2·68	0·46°	2·17	0·0°	1·79	0·03°	1·46
15·98	17·2	15·95	15·19	15·98	12·84	15·95	10·78	16·00	9·49	15·97	8·06
25·00	38·6	25·00	32·9	25·00	27·0	25·00	24·02	25·00	21·4	25·00	18·59
39·75	116·5	39·8	101·2	39·70	88·3	39·75	77·6	39·75	73·3	39·8	63·7
Solvent G.		Solvent H.		Solvent J.		Solvent K.		Solvent M.		Solvent N.	
0·0	1·78	0·46	1·29	0·35	0·932	0·0	0·731	0·0	0·183	0·0	7·8
16·00	9·20	15·98	6·54	15·98	5·12	16·00	4·14	16·0	1·17	16·0	29·3
25·00	21·05	25·00	15·3	25·00	12·03	25·00	10·02	25·00	3·56	25·0	64·0
39·75	68·4	39·68	55·5	39·7	45·6	39·97	39·6	39·75	15·57	39·7	162

* All constants are in g.-mol./l.-sec. units.

The viscosity data for alcohol–water mixtures given in Table I were taken from the International Critical Tables. Those for the alcohol–acetone–water mixtures were specially determined by Messrs. Vicary and Rowse.

Alkaline hydrolysis of methyl acetate. The method was essentially the same as for ethyl benzoate, but, since the reaction is much faster, the plan described by Newling and Hinshelwood (*loc. cit.*) for dealing with rapid reactions was followed. In solutions containing ethyl alcohol, a gradual direct conversion of the methyl ester into the ethyl ester seems to occur and results in a fall in the rate of hydrolysis. To obtain the true hydrolysis rate in such solutions, the initial rates of reaction were taken from curves. The results are collected in Table III.

Alkaline hydrolysis of ethyl bromide. The results are given in Table IV. In Fig. 2 an earlier result for an alcoholic solution is included (Grant and Hinshelwood, J., 1933, 258).

Formation of methylpyridinium iodide. The method of estimating ionisable halogen could not be used, since the salt is soluble in the solvents used and cannot be separated from the

TABLE III.

Hydrolysis of methyl acetate.

Solvent A.		Solvent K.		Solvent H_2O.		Solvent A.		Solvent K.		Solvent H_2O.	
Temp.	$k \times 10^2$.	Temp.	$k \times 10^2$.	Temp.	$k \times 10^2$.	Temp.	$k \times 10^2$.	Temp.	$k \times 10^2$.	Temp.	$k \times 10^2$.
0·0°	1·41	0·0°	0·376	0·0°	2·98	25·0°	8·90	25·0°	3·31	25·0°	15·24
16·0	5·21	16·0	1·52	16·0	9·53	39·7	22·2	39·7	12·0	39·7	32·6

TABLE IV.

Hydrolysis of ethyl bromide.

Solvent A.		Solvent H.	
Temp.	$k \times 10^4$.	Temp.	$k \times 10^4$.
25·0°	0·568	25·0°	0·471
39·9	2·66	39·9	2·69
60·1	16·60	60·1	20·2
80·4	80·1	80·4	105·0

TABLE V.

Formation of methylpyridinium iodide.

Solvent A.		Solvent H.	
Temp.	$k \times 10^4$.	Temp.	$k \times 10^4$.
25·0°	1·76	25·00°	0·53
39·9	6·2	39·85	2·11
60·1	27·8	60·0	11·5
80·4	90·8	80·4	59·5

unchanged methyl iodide, which reacts with silver nitrate. Accordingly, the pyridine was determined by titration with acid according to the procedure of Fawcett and Gibson (J., 1934, 396), the indicator consisting of a mixture of equal volumes of aqueous 0·1% methyl-orange and 0·02% methylene-blue. The results are collected in Table V.

(3) *Discussion of Experimental Results.*

Before attempting any general interpretation of these results, we must consider whether the values of E derived from the Arrhenius equation represent the true activation energies.

It should be emphasised at the outset that no inclusion in P of any term variable exponentially with $1/T$ is significant. Such a temperature variation always indicates a process requiring a critical energy. A term of this kind would be measured in determining the temperature coefficient, as part of the exponential containing the activation energy, and since the energy represented by the extra term is necessary for the reaction, it is in reality simply a part of the activation energy, whatever formal designation it may receive. (See, *e.g.*, Hückel, *Z. physikal. Chem.*, 1936, *A*, **178**, 113, who includes certain energies of orientation in a P-term.)

It has been suggested that observed activation energies should in certain cases be corrected for variation of the viscosity of the medium with temperature (Jowett, *Phil. Mag.*, 1929, **8**, 1059). It is doubtful whether such corrections would be relevant here, but even if applied they would not explain the results, since they would affect the various activation energies in an irregular way, and give rise to a less orderly rather than a simpler picture. For example, in the range of mixtures alcohol–acetone–water the corrections would accentuate the variation of E with composition, while in the alcohol–water series they would diminish it (see Table I). Thus application of the correction in the former case would accentuate the increase of log PZ through the series.

If the total activation energy contains any considerable contribution from electrostatic potential energies, then the value of P depends upon the dielectric constant and its temperature variation, a matter which becomes very important in reactions between multiply charged ions (Moelwyn-Hughes, *Proc. Roy. Soc.*, 1936, *A*, **157**, 667). The variation in dielectric constant over a large part of the range of solvents we have used is small: and in any case calculation from the formulæ used by Moelwyn-Hughes shows that the changes in P arising even from much greater variations would, for reactions of the type, with which we are concerned, involving nothing more than ion–dipole or dipole–dipole forces, be of a lower order of magnitude than those observed.

The values of E and $\log_{10} PZ$ are collected in Table VI. In Fig. 2 log PZ is plotted against $1/\sqrt{E}$. This method of plotting is adopted because it is indicated by the theoretical considerations of Section (4). The essential regularity is that log PZ is proportional to

TABLE VI.

Solvent.	E.	$\log_{10} PZ$.	Solvent.	E.	$\log_{10} PZ$.
Reaction : $Ph{\cdot}CO_2Et + NaOH$.			Reaction : $CH_2{\cdot}CO_2Me + NaOH$.		
A	14,010	7·875	A	11,680	7·545
B	14,700	8·335	K	15,000	9·60
C	15,080	8·53	O	10,450	6·87
D	15,250	8·60			
E	15,800	8·96	Reaction : $EtBr + \bar{O}H$.		
F	15,970	9·02	A	18,550	9·40
G	15,640	8·82	H	20,150	10·50
H	16,070	9·03			
J	16,570	9·28	Reaction : $C_5H_5N + CH_3I$.		
K	16,980	9·51			
M	19,030	10·55	A	14,700	7·29
N	12,830	7·195	H	18,200	9·05

some simple function of E. If this function were chosen differently, the correlation would be little altered. For example, if we plot E directly, we still obtain an approximately straight line, provided that the logarithmic form of PZ is retained.

Since the correlation of PZ and E is shown by two examples of ester hydrolysis, in which the water molecules probably participate in the reaction, by the hydrolysis of ethyl bromide which is probably a direct attack of the hydroxyl ion on the halide, and by an example of quaternary ammonium salt formation the mechanism of which is different again, explanation in rather general terms not involving the specific properties of individual systems seems to be called for.

(4) *Theoretical Considerations.*

The following considerations seem to show that a correlation between PZ and E similar to that found is not merely explicable but should even be rather common, as, indeed, scattered indications in the literature had suggested.

We base our theory upon the following picture of a chemical reaction between two molecules. They must come together possessing the activation energy and constitute a preactivated collision complex (Hinshelwood, J., 1935, 1111). The life of this is terminated either by the separation of the constituents, or by deactivation in a collision, or by chemical transformation. The condition for chemical transformation is that existing bonds must be broken and new ones formed. Generally, a bond will only be broken when the atoms it joins are near the extremes of their amplitudes; while new bonds will only be formed when the atoms which they are to unite are at appropriate distances and possess suitable relative velocities. These conditions will in general be fulfilled only in a narrow range of the complicated pattern of motions executed by the system. On the average, therefore, many cycles of the separate vibrations may have to be traversed before the right region of the complete Lissajou figure for the system is reached.

Let the average time which elapses between the formation of the preactivated collision complex and the reversal of this process be θ. In the majority of cases the attainment of the right phase for reaction demands a longer time than this, which we call t, and no reaction occurs. The chance that the preactivated complex survives for this time is, according to well-established statistical principles,

$$W = e^{-t/\theta} \qquad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \qquad (1)$$

t is the time required for the completion of a certain fraction of the complete period of a complex internal motion, which in general will involve a considerable number, n, of cycles of vibration of one of the reacting bonds. If the frequency of the latter is ν, $t = n/\nu$. Thus the probability of reaction is proportional to $e^{-n/\nu\theta}$.

If the structure of the molecules remains constant but the bond strengths are changed by substitution, or by the influence of the medium, ν will vary, and E, the activation energy, will vary also. On the whole, if bond strengths increase, both ν and E will increase together. If we write $\nu = f(E)$, then the rate of reaction becomes

$$k = A \,.\, e^{-n/\theta f(E)} \,.\, e^{-E/RT}$$

whence $$\log k = \log A - n/\theta f(E) - E/RT = \log PZ - E/RT$$

whence $$\log PZ = \text{constant} - n/\theta f(E) \qquad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \qquad (2)$$

When changes in E are small compared with $f(E)$, this approximates to

$$\Delta \log PZ = B \,.\, \Delta E, \text{ where } B \text{ is a constant.}$$

The exact relation between ν and E is difficult to determine, and from our point of view is a secondary matter.

To give the expression a definite form, however, we will set the activation energy proportional to the force constant of the link, *i.e.*, to the square of the frequency.

If ν_0 and E_0 are the values for some standard reaction of a series, then for another member $\nu = \nu_0\sqrt{E/E_0}$. The chance of reaction will now be $e^{-n\sqrt{E_0/E}/\theta\nu_0}$ and the rate of reaction will be

$$A \,.\, e^{-E/RT} \,.\, e^{-n\sqrt{E_0/E}/\theta\nu_0}$$

We then have

$$\log k = \log A - n\sqrt{E_0/E}/\theta\nu_0 - E/RT = \log PZ - E/RT$$

whence

$$\log PZ = \text{const.} - n\sqrt{E_0/E}/\theta\nu_0 \qquad . \quad . \quad . \quad . \quad . \quad . \quad . \qquad (3)$$

For small changes this reduces as before to

$$\Delta \log PZ = B' \,.\, \Delta E$$

The constants n, E_0, and ν_0 depend primarily on the nature of the reaction, whereas θ will depend principally on the medium.

Since the function of E appears in an exponential, it is not easy to determine empirically what the best function is, the exponential itself being responsible for the characteristic form of the variation. The essential part of the present theory is that we expect the

exponential relation of equation (1). Some alternative theories which we explored did not lead to an exponential relation but predicted that PZ itself rather than its logarithm should increase comparably with E.

(5) *Comparison with Experiment.*

Only when t is appreciably greater than θ in equation (1) should the correlation between PZ and E be observable. When t is much less than θ, equation (1) approximates to $W = 1$, and PZ is no longer dependent upon E. Thus two main types of behaviour are to be expected. The factors making for a large value of θ, and therefore for a constant P, are the formation of a fairly stable collision complex, infrequency of collisions which might deactivate the complex, and poor energy transfer in such potentially deactivating collisions. On the other hand, simplicity of the reacting system tends to diminish t, which has the same result as increasing θ. In this connexion it must be remembered that a reaction in an active solvent, involving as it must do much interference by the solvent molecules, may require the fulfilment of a much more complicated set of conditions than its chemical equation would suggest.

Among reactions which have been investigated, three types of behaviour have been distinguished. In the first, the change of E is accompanied by the sort of change in PZ to be expected from the exponential relation (1).

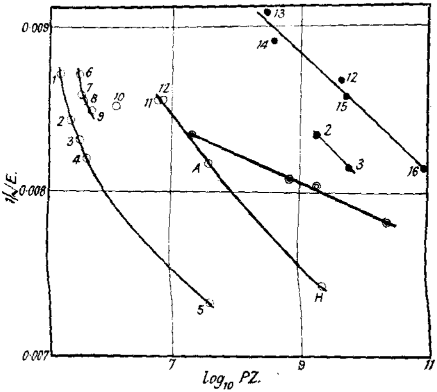
Examples of the following kinds have from time to time been noted: Heterogeneous reactions (see Storch, *J. Amer. Chem. Soc.*, 1935, **57**, 1395); unimolecular reactions in different solvents, *e.g.*, decomposition of acetonedicarboxylic acid (Wiig, *J. Physical Chem.*, 1928, **32**, 961), and the rearrangement of triazoles (Dimroth, *Annalen*, 1910, **373**, 367); unimolecular reactions of series of related compounds such as substituted malonic acids (Bernoulli and Wege, *Helv. Chim. Acta*, 1919, **2**, 511); bimolecular reactions such as the formation of allylpyridinium bromide in different solvents (Hawkins, J., 1922, **121**, 1170), esterification of acids in different alcohols (Hinshelwood and Legard, J., 1935, 587), formation of sulphonium salts in different solvents (Syrkin and Gladischev, *Acta Physicochim. U.R.S.S.*, 1935, **2**, 291); hydrolysis of different arylsulphuric acids in water (Burkhardt, Horrex, and Jenkins, J., 1936, 1649). In the examples quoted, the correlation is fairly well marked (Fig. 4): in others it is detectable though less definite.

A conspicuous part is played by change in medium, as in the examples given in the present paper. In this connexion the results of Gibson, Fawcett, and Perrin (*Proc. Roy. Soc.*, 1935, *A*, **150**, 223) are of much interest. These authors found that in the formation of quaternary ammonium salts large increases in the hydrostatic pressure on the medium could produce increases in the activation energy accompanied by increases in P so great as to increase the reaction rate by a large factor (Fig. 3). From one point of view, increased hydrostatic pressure might be thought of as increasing the number of deactivating impacts and decreasing θ, but the predominating effect at really high pressures will be a different one: the system has become so tightly packed that the components of the collision complex may be actually held together by surrounding solvent molecules in such a way as to increase θ very considerably. For the reverse reaction, which is a unimolecular decomposition, this effect is of no advantage, and pressure produces no increase in rate, but a slight retardation.

In certain well-defined cases (Williams and Hinshelwood, J., 1934, 1079; Ingold and Nathan, J., 1936, 222; Bradfield, *Chem. and Ind.*, 1932, **51**, 254) the correlation of P and E does not appear at all, the change in velocity being due almost entirely to change in the activation energy. This would have been most easily understood if P for these cases were near unity, θ being large or t small. But for reactions such as the benzoylation of substituted amines, P is of the order 10^{-7}. This shows that the exponential (1) is by no means the only factor contained in P: there must be correct orientation of the approaching molecules; they must fit together to form the collision complex; they must reach the right internal phase; and finally, a stabilising collision may be necessary in some cases to prevent the reversion of the product. Our attention is drawn to the last of these factors by examples where P varies without corresponding change in E. The study of the form-

ation of methylpyridinium iodide in a series of solvents (Pickles and Hinshelwood, J., 1936, 1353) led to the following results: in a series of substituted benzene derivatives E remains nearly constant, P increasing with the polarity of the solvent. For a series of inert solvents E increases and there is an accompanying increase in P. We have now found that for a series of solvents of about the same polarity as the most polar of those used by Pickles and Hinshelwood there is the usual correlation of P and E. The more complete picture would therefore seem to be as follows: E and log PZ increase together in a simple manner for solvents of about the same polarity, but the line expressing this correlation shifts towards higher values of P the greater the polarity of the solvent. This view is supported by certain data scattered in the literature (Fig. 3). With regard to the interpretation of this effect, we do not propose to do more at the moment than suggest that it might be due to the necessity for a suitable solvent collision to stabilise the polar

FIG. 3.



Solvents.—1, Chloroform. 2, Benzene. 3, Toluene. 4, Mesitylene. 5, Carbon tetrachloride. 6, Anisole. 7, Dioxan. 8, Bromobenzene. 9, Chlorobenzene. 10, Iodobenzene. 11, Benzonitrile. 12, Nitrobenzene. 13, Acetophenone. 14, *p*-Nitrotoluene. 15, Acetone. 16, Ethyl alcohol.

Open circles: Formation of methylpyridinium iodide (Pickles and Hinshelwood, *loc. cit.*).

Shaded circles: Formation of allylpyridinium iodide (Hawkins, J., 1922, **121**, 1170).

Double circles: Formation of ethylpyridinium iodide under high pressures (Gibson, Fawcett, and Perrin, *loc. cit.*).

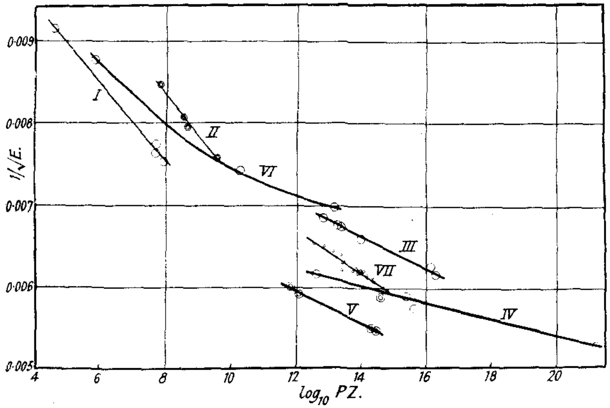
product in the manner indicated in a previous paper (Hinshelwood, *Trans. Faraday Soc.*, 1936, **32**, 970). If change in hydrostatic pressure enhances this effect continuously, as well as exerting the influence discussed above, the very considerable rate of increase of P with E found by Gibson, Fawcett, and Perrin becomes more easily understandable.

(6) *Collision Rates; Limiting Values of* P.

It will be observed that in Figs. 2, 3, and 4 the lines might be extrapolated to obtain the values of PZ when $1/\sqrt{E} = 0$. This gives the value which PZ would possess if the time required for the right phase to be reached were negligible, and gives us Z multiplied by the probability that the other conditions are favourable. Since the curves are not quite linear, the extrapolation is very rough, but the values of PZ so obtained would always be several powers of 10 greater than that corresponding to the gas collision number with $P = 1$, which is of the order 10^{11}. This would suggest one of two things: either that

Z is considerably greater than the value for the gas, or that $P = 1$ loses any significance as a limiting value. That this limit has no absolute significance is already shown by several facts : there is a complete range of P values filling the region between 10^{-8} and 1 (Hinshelwood and Winkler, J., 1936, **371**) ; there are several examples of bimolecular changes with P greater than 1, *e.g.*, the hydrolysis of the arylsulphuric acids (Burkhardt, Horrex, and Jenkins, *loc. cit.*) ; the line in Fig. 2 for the hydrolysis of ethyl bromide shows no signs of bending over at $P = 1$ ($PZ = 10^{11}$—10^{12}). The only obvious way of explaining values of P greater than unity is by the introduction of formulæ in which internal degrees of freedom contribute to the activation rate, as in unimolecular reactions. Now, the extrapolated values correspond to a state of affairs where the collision complex is allowed all

FIG. 4.



I. Formation of methyldiethylsulphonium bromide (Syrkin and Gladischev, *Acta Physicochim. U.R.S.S.*, 1935, **2**, 291).
II. Influence of pressure on esterification of acetic anhydride (Williams, Perrin, and Gibson, *Proc. Roy. Soc.*, 1936, *A*, **154**, 684).
III. Decomposition of acetonedicarboxylic acid (Wiig, *J. Physical Chem.*, 1928, **32**, 961).
IV. Isomerisation of methyl 5-hydroxy-1-benzyltriazole-4-carboxylate (Dimroth, *Annalen*, 1910, **373**, 367).
V. Decarboxylation of substituted malonic acids (Bernoulli and Wege, *Helv. Chim. Acta*, 1919, **2**, 511).
VI. Esterification of methyl alcohol by different acids (Hinshelwood and Legard, J., 1935, 587).
VII. Acid hydrolysis of phenylsulphuric acids (Burkhardt, Horrex, and Jenkins, J., 1936, 1649).
V, VI, *and* VII *refer to series in which the nature of the reactants is modified, the others to changes* in the medium.

the time it requires to undergo re-arrangement : this differs little from the state of affairs in a unimolecular reaction. The rather rare experimental cases where P is actually greater than unity may involve collision complexes with abnormally long lives, and thus represent a true transition between bimolecular and unimolecular reactions.

Fig. 4 shows that a dependence of P upon E is found for unimolecular reactions also, and here P rises to very high values. In the light of all these considerations the principal factors differentiating one case from another are simply the relative time intervals between activation, deactivation or resolution of the activated system, and the completion of the chemical transformation.

If we do not wish to admit that P can reach values considerably greater than unity in

exceptional cases, then we must suppose that the collision number Z itself reaches values considerably greater than the gas-kinetic values.* The theory of collision rates in solution is difficult, but the calculations of Leontovitch (*Z. Physik*, 1928, **50**, 58), as well as the experiments of Rabinowitch and Wood (*Trans. Faraday Soc.*, 1936, **32**, 1381) with models, seem to show that the order of magnitude, at least, should be the same as in the gas phase. Both approaches, however, deal with somewhat idealised systems, and it is possible that with real solvents considerable divergences might occur. If, for example, owing to swarm formation, parts of the solvent became impenetrable to solute molecules, the collision rate in the space remaining would be increased. But it is hardly possible to say much that is definite about this at present.

SUMMARY.

For four bimolecular reactions in a range of solvents containing alcohol, acetone, water, and dioxan, a correlation is found between the activation energy and the temperature-independent factor of the Arrhenius equation.

These results, taken in conjunction with data from the literature, lead us to the conclusion that the correlation is unlikely to be accidental, and an explanation is proposed based upon general statistical principles and upon the assumption of a time interval between activation and reaction.

Factors determining the probability of reaction are discussed.

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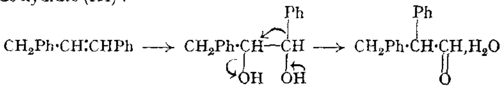
121. *αβ-Diphenylpropaldehyde.*

By HAROLD BURTON and C. W. SHOPPEE.

αβ-DIPHENYLPROPALDEHYDE has been described by Stoermer, Thier, and Laage (*Ber.*, 1925, **58**, 2607) as the monohydrate, a crystalline solid, m. p. 116°, possessing reducing properties, and characterised by a semicarbazone, m. p. 189° (decomp.). They obtained the substance by oxidation of αγ-diphenylpropene (I) with potassium permanganate in acetone solution in the presence of 2*N*-sulphuric acid, an observation which was interpreted by the suggestion that the intermediate glycol (II) underwent a pinacolic change to give the aldehyde hydrate (III):



(I.) (II.) (III.)

It is recorded, however, that the substance by oxidation with ammoniacal silver nitrate, in spite of the ready production of silver, failed to yield the expected αβ-diphenylpropionic acid, m. p. 96°.

After several unsuccessful attempts, using various methods, we eventually obtained the aldehyde from *αβ-diphenylpropanilide* (IV) by reduction of the corresponding iminochloride (V) with stannous chloride and hydrolysis of the resulting aldimine (Sonn and Müller, *Ber.*, 1919, **52**, 1927). *αβ-Diphenylpropaldehyde* (VI) is a faintly yellow oil, b. p. 170°/11 mm., which crystallises after some weeks, and on recrystallisation forms colourless plates, m. p. 54°. It is oxidised by silver oxide to αβ-diphenylpropionic acid, and is characterised by a *semicarbazone*, m. p. 125°. It gives two (presumably stereoisomeric) 2 : *4-dinitrophenylhydrazones*, m. p. 148—152° and 199°; the lower-melting form is obtained from the freshly distilled liquid aldehyde, and, since the m. p. is not sharp and tends to rise

* A question of terminology arises here. From considerations based upon the transition-state method some authors have concluded that the " collision " factor is greater in solution than in the gas. By collision factor they have meant the temperature-independent factor of the Arrhenius equation, *i.e.*, our *PZ*, so their statement might refer either to *Z* or to *P*.

by repeated crystallisation, may contain some of the higher-melting form, which is obtained from the crystalline aldehyde. The aldehyde condenses readily with malonic acid in pyridine–piperidine to furnish a good yield of *γδ-diphenyl-Δ^{α}-pentenoic acid*, m. p. 89°.

$$CH_2Ph{\cdot}CHPh{\cdot}CO{\cdot}NHPh \xrightarrow{PCl_5} CH_2Ph{\cdot}CHPh{\cdot}CCl{:}NPh \xrightarrow[\text{and hydrolysis}]{SnCl_2} CH_2Ph{\cdot}CHPh{\cdot}CHO$$

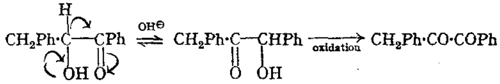
(IV.) (V.) (VI.)

Jarrousse (*Compt. rend.*, 1935, **201**, 676) records the production, from α-hydroxy-γ-keto-β-phenyl-α-benzylglutaric acid (VII) by oxidation with permanganate, of αγ-diketo-βδ-diphenylvaleric acid (VIII), which easily loses carbon dioxide to give a substance, m. p. 114°. This was considered to be β-keto-αγ-diphenylbutaldehyde (IX), but is actually identical with the product, m. p. 116°, of Stoermer, Thier, and Laage. It has been shown

(VII.) $CH_2Ph{\cdot}C(OH)(CO_2H){\cdot}CHPh{\cdot}CO{\cdot}CO_2H$ $CH_2Ph{\cdot}CO{\cdot}CHPh{\cdot}CO{\cdot}CO_2H$ (VIII.)

$CH_2Ph{\cdot}CO{\cdot}CHPh{\cdot}CHO$ (IX.)

(Jarrousse, *Compt. rend.*, 1936, **203**, 259) to be phenylacetylphenylcarbinol (X) (previously prepared by Kohler and Timball, *J. Amer. Chem. Soc.*, 1934, **56**, 729), since it can be obtained from the isomeric benzoylbenzylcarbinol (XI) (McKenzie, Martin, and Rule, J., 1914, **105**, 1589) by pinacolic change in the presence of alkali (compare Shoppee, J., 1928, 1662), and by oxidation with Nessler's reagent it gives phenyl benzyl diketone (XII).



(XI.) (X.) (XII.)

We also have shown that the supposed aldehyde hydrate, m. p. 116°, is phenylacetylphenylcarbinol (X) by analysis of it and its derivatives, and have confirmed the production of phenyl benzyl diketone (XII) by oxidation with Nessler's reagent in dioxan, and by preparation of the quinoxaline (Widman, *Ber.*, 1916, **49**, 484) of (XII). Oxidation of (X) with Fehling's solution or phenylhydrazine acetate at 100° was unsatisfactory, and an earlier attempt with Nessler's reagent in acetone furnished a compound, $C_{18}H_{16}O_2$, which we consider to be the iso*propylidene* derivative, $CPh({:}CMe_2){\cdot}CO{\cdot}COPh$, since ozonolysis gave acetone, phenylglyoxylic acid, and benzoic acid.

Phenylglyoxylic acid condenses extremely easily with alcoholic *o*-phenylenediamine to give the *compound* (XIII or XIV); owing to its insolubility and sharp m. p. (247°), this substance should be valuable for the microchemical detection of phenylglyoxylic acid.

(XIII.) (XIV.)

EXPERIMENTAL.

αβ-*Diphenylpropaldehyde* could not be obtained by reduction (Adams's catalyst, various solvents, and pressures up to 100 atms.) of α-phenylcinnamaldehyde, m. p. 97—98° [2 : 4-*dinitrophenylhydrazone*, m. p. 240—241° (Found: C, 65·0; H, 4·0. $C_{21}H_{16}O_4N_4$ requires C, 64·9; H, 4·1%)]. αβ-Diphenylpropionitrile, prepared from benzyl chloride and sodiophenylacetonitrile in liquid ammonia or by the method of Janssen (*Annalen*, 1889, **250**, 129), b. p. 208—210°/23 mm., m. p. 58° after crystallisation from carbon tetrachloride–ligroin, could not be reduced by Stephen's method (J., 1925, **127**, 1874); it was smoothly and completely hydrolysed by 50% sulphuric acid (20 parts) and glacial acetic acid (15 parts) in 24 hours to αβ-diphenylpropionic acid, m. p. 96° after crystallisation from ligroin (b. p. 60—80°). The acid was converted by treatment with thionyl chloride (von Auwers and Auffenberg, *Ber.*, 1919, **52**, 108) into αβ-diphenylpropionyl chloride, which condensed with aniline (2 mols.) to give αβ-*diphenylpropanilide*, m. p. 166°, colourless needles from alcohol (Found: C, 83·8; H, 6·4. $C_{21}H_{19}ON$ requires C, 83·7; H, 6·3%); it is not necessary to distil the acid chloride, as the crude product remaining after removal of the excess of thionyl chloride may be used to form the anilide without disadvantage (compare Rupe and Kerkovius, *Ber.*, 1912, **45**, 1399). The anilide (25 g.) and

phosphorus pentachloride (18 g.) were heated in tetrachloroethane for 1 hour at 140°; after removal of phosphorus oxychloride in a vacuum, the iminochloride, redissolved in tetrachloroethane, was added to 70 g. of anhydrous stannous chloride dissolved in ether (350 c.c.) saturated with hydrogen chloride at 0°. After standing overnight, the yellow crystalline stannichloride was filtered off, washed with ether, and hydrolysed with hot 2*N*-hydrochloric acid (500 c.c.); extraction with ether and subsequent drying (calcium chloride), evaporation, and distillation gave αβ-diphenylpropaldehyde as a pale yellow oil (9 g.), b. p. 170°/11 mm. (Found: C, 85·6; H, 6·8%). The aldehyde solidified after some weeks, and two recrystallisations from ligroin (b. p. 40—60°) gave colourless plates, m. p. 54° [Found: C, 85·6; H, 6·3; *M* (Rast), 199. $C_{15}H_{14}O$ requires C, 85·7; H, 6·7%; *M*, 210]. It was not readily volatile in steam and did not give a crystalline bisulphite compound. The *semicarbazone* formed colourless felted needles from dilute alcohol, m. p. 124—125° (Found: C, 72·0; H, 6·5; N, 15·5. $C_{16}H_{17}ON_3$ requires C, 71·9; H, 6·4; N, 15·7%); the same semicarbazone was produced both from the freshly distilled liquid aldehyde and from a crystalline specimen. The aldehyde appears to afford two orange-yellow 2 : 4-*dinitrophenylhydrazones*; by the procedure of Brady (J., 1931, 756) the freshly distilled liquid aldehyde gave one form, which separated from ethyl acetate–ethyl alcohol in yellow plates, m. p. 148—152° (Found: C, 64·6; H, 4·8; N, 13·6. $C_{21}H_{18}O_4N_4$ requires C, 64·6; H, 4·65; N, 14·4%); the m. p., however, rose on further crystallisation, *e.g.*, a specimen, m. p. 164°, gave C, 64·4; H, 5·0; N, 13·7%. The crystalline aldehyde gave another form, which crystallised from ethyl acetate–ethyl alcohol in orange-yellow plates, m. p. 199° (Found: C, 63·8; H, 4·5; N, 15·1%).

γδ-Diphenyl-Δ^α-pentenoic Acid.—αβ-Diphenylpropaldehyde (9·0 g.) was condensed with a 10% excess of malonic acid (4·5 g.) in 40 c.c. of pyridine containing 4 drops of piperidine, by standing overnight at 15°, followed by heating on the steam-bath for 3 hours. The mixture having been poured into ice–hydrochloric acid, extraction with ether, re-extraction with sodium carbonate solution, acidification of the alkaline extract, and ether extraction of the last-named gave a solution the oil obtained from which by drying (calcium chloride) and evaporation was kept in a vacuum over potash. By removal of traces of acetic acid, solidification of the product readily occurred; after crystallisation from ligroin containing a trace of ether, and subsequently from ligroin (b. p. 60—80°), *γδ-diphenyl-Δ^α-pentenoic acid* (8 g.) formed colourless prisms, m. p. 89°, which decolorised alkaline permanganate instantly [Found: C, 81·0; H, 6·4; *M* (Rast), 223, 224. $C_{17}H_{16}O_2$ requires C, 81·0; H, 6·4%; *M*, 252].

Phenylacetylphenylcarbinol (X).—Diphenylpropene, readily obtained in good yield from phenylacetaldehyde by the method of Stoermer, Thier, and Laage (*loc. cit.*), was oxidised with potassium permanganate in acetone in the presence of 2*N*-sulphuric acid at 5—10° according to the directions of these authors. Filtration, and evaporation of the acetone filtrate gave an oil which crystallised overnight; after being pressed on porous porcelain and crystallised from alcohol, the α-ketol formed colourless plates, m. p. 116° [Found: C, 79·8; H, 6·0; *M* (Rast), 206. Calc. for $C_{15}H_{14}O_2$: C, 79·7; H, 6·2%; *M*, 226]. It formed a *semicarbazone* (described incorrectly by Stoermer, Thier, and Laage), which separated from alcohol in plates, m. p. 191—192° (decomp.) (Found: C, 68·0; H, 6·15. $C_{16}H_{17}O_2N_3$ requires C, 67·8; H, 6·05%), and a 2 : 4-*dinitrophenylhydrazone*, which formed orange plates from ethyl acetate–alcohol, m. p. 164—164·5° (Found: C, 62·7; H, 4·8; N, 13·6. $C_{21}H_{18}O_5N_4$ requires C, 62·1; H, 4·5; N, 13·8%); the 3 : 5-dinitrobenzoate could not be obtained. The ketol readily reduced ammoniacal silver nitrate to silver, and mercuric salts to mercury.

Phenyl Benzyl Diketone (XII).—Phenylacetylphenylcarbinol (1·0 g.), dissolved in dioxan (25 c.c.), was shaken with Nessler's reagent (100 c.c.) at 15° for 1 hour. The resulting solution was repeatedly extracted with ether, and the extract washed with water, dried (sodium sulphate), and evaporated. The yellow oil was treated with *o*-phenylenediamine in hot alcohol, whence, by cooling, 2-phenyl-3-benzylquinoxaline separated in yellow needles, m. p. 97°, unchanged by crystallisation (Found: C, 84·7; H, 5·6; N, 9·9. Calc. for $C_{21}H_{16}N_2$: C, 85·1; H, 5·4; N, 9·5%). The diketone appears to exist as the diketo-form even in the presence of potassium hydroxide, since acidification of the aqueous liquor and further ether extraction afforded only a trace of oil giving a brown-purple colour with aqueous-alcoholic ferric chloride.

When the above oxidation was performed with acetone in place of dioxan, the neutral product obtained consisted of an oil which solidified on scratching with evolution of heat. The substance was re-dissolved in ether, the solution decanted from a trace of tarry matter and evaporated, and the solid residue crystallised from carbon tetrachloride–ligroin (b. p. 80—100°); the *δε-diketo-γε-diphenyl-β-methyl-Δ^β-pentene* formed pale yellow prisms, m. p. 123° [Found: C, 82·05; H, 6·12; *M* (Rast), 241. $C_{18}H_{16}O_2$ requires C, 81·8; H, 6·1%; *M*, 264]. A quinox-

aline could not be obtained. Ozonolysis in chloroform solution, and decomposition of the ozonide with hot water, gave, amongst the more volatile products, acetone (identified as iodoform with iodine and ammonia in the cold), phenylglyoxylic acid (characterised by the condensation product, m. p. 247°, with *o*-phenylenediamine described below), and benzoic acid.

3-*Hydroxy-2-phenylquinoxaline* (3-*Keto-2-phenyl-3* : 4-*dihydroquinoxaline*) (XIII or XIV).—Phenylglyoxylic acid, obtained by oxidation of acetophenone with alkaline permanganate at 5—10° (Glücksman, *Sitzungsber. Akad. Wiss. Wien*, 1890, **99**, 273), readily condensed with *o*-phenylenediamine in alcohol to give the *hydroxyphenylquinoxaline*, which formed pale yellow needles from alcohol, m. p. 247° (Found: C, 75·4; H, 4·6. $C_{14}H_{10}ON_2$ requires C, 75·7; H, 4·55%).

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122. *Gluco-ascorbic Acid.*

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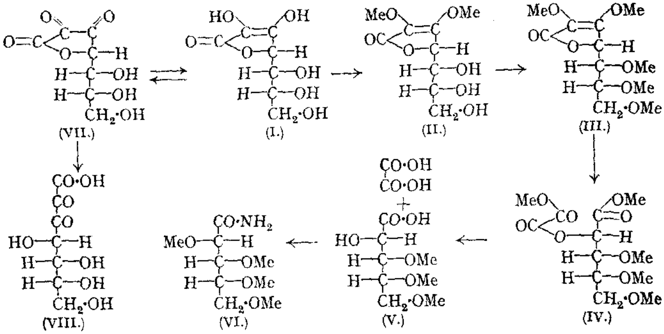
THE constitution of *l*-ascorbic acid (vitamin C) as the enolic form of 2-keto-*l*-gulofuranolactone has been definitely established by ozonisation of its tetramethyl ether and identification of the oxidation product (Herbert, Hirst, Percival, Reynolds, and Smith, J., 1933, 1270). It was shown that a γ-lactone ring is present in *l*-ascorbic acid and by analogy the same ring system has been assigned to the numerous analogues of ascorbic acid which have been obtained synthetically. Although this assumption is in full agreement with the properties of the various analogues, the possibility that ring systems of the pyranose type also may occur in the ascorbic acid series has to be kept in mind and in a subsequent paper it will be shown that such structures do in fact exist in the series. It is necessary, therefore, to establish by definite chemical transformations the nature of the ring system present in any particular analogue and this paper is concerned with the constitution and properties of *d*-gluco-ascorbic acid. Proof is now given of the correctness of the structure (I) provisionally assigned to this substance in earlier communications.

The different stages of the investigation may be summarised as follows. Improved methods are given for the preparation of *d*-gluco-ascorbic acid from *d*-glucosone *via* the iminoglucoascorbic acid obtained by addition of hydrogen cyanide to the osone (Haworth, Hirst, Jones, and Smith, J., 1934, 1192). It is shown that *d*-gluco-ascorbic acid reacts with diazomethane, giving successively the 3-*monomethyl* ether and the 2 : 3-*dimethyl* ether (II), the mode of formation and the properties of both derivatives being such as to make it certain that no structural change occurs during their formation from *d*-gluco-ascorbic acid. The remaining hydroxyl groups can be methylated without opening of the lactone ring and the product is the fully substituted 2 : 3 : 5 : 6 : 7-*pentamethyl* d-*gluco-ascorbic acid* (III). The latter substance reacts with ozone, giving a neutral ester (IV) which on hydrolysis gives oxalic acid and 3 : 4 : 5-*trimethyl arabonic acid* (V). The identity of the last substance was proved in the following way. It was a derivative of *d*-arabonic acid, because methylation of the corresponding ester (*methyl* 3 : 4 : 5-*trimethyl arabonate*) gave *methyl* 2 : 3 : 4 : 5-*tetramethyl* d-*arabonate*, recognised as the crystalline *amide* (VI), which was compared with its enantiomorph (2 : 3 : 4 : 5-*tetramethyl* l-*arabonamide*), prepared specially for this work by methylation of *l*-arabonic acid. Since the *trimethyl* d-*arabonamide* obtained from *d*-gluco-ascorbic acid gave a strong positive Weerman reaction with sodium hypochlorite, it contained a hydroxyl group attached to C_2. It follows that the three methyl groups must of necessity be attached to C_3, C_4, and C_5, and the identity of the amide is thereby established.

The location of the hydroxyl group at C_4 in the trimethyl *d*-arabonamide isolated from methylated gluco-ascorbic acid fixes the point of attachment of the ring in gluco-ascorbic acid and shows that this analogue of ascorbic acid is a γ-lactone (I). The various transformations which furnish the proof of structure are summarised in the scheme on p. 550.

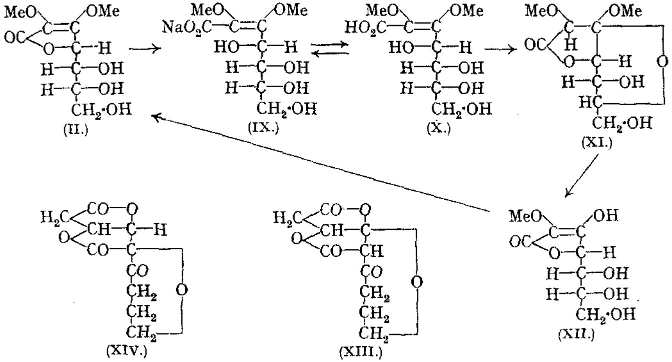
It follows that a γ-lactonic structure must apply also to the enantiomorph of *d*-gluco-ascorbic acid, *l*-gluco-ascorbic acid, the preparation of which from *l*-arabinose is described in the experimental section. The *d*-form has no antiscorbutic activity, but the *l*-form is

slightly active (Reichstein, *Nature*, 1934, **134**, 724; Zilva, *Biochem. J.*, 1935, **29**, 1612). The active isomeride has one feature in common with all the other analogues of ascorbic acid which show antiscorbutic powers, namely, that the lactone ring is on the right when the formula is written in accordance with the Fischer convention.



Further details of the properties of the substances referred to above are recorded in the experimental section. These require no further comment except in the case of 2 : 3-dimethyl gluco-ascorbic acid, the behaviour of which is anomalous in certain respects. The dimethyl derivative does not react with alcoholic ammonia and no derivative can be obtained corresponding to the amide readily formed from dimethyl ascorbic acid. The reaction of 2 : 3-dimethyl gluco-ascorbic acid with alkali proceeds normally with opening of the lactone ring and salt formation (IX), and the open-chain derivative possesses no selective absorption. On acidification, an acid (X) is temporarily produced, but if its isolation is attempted, lactonisation occurs and a substance is obtained with properties similar to those of the *iso*dimethyl ascorbic acid which is formed from dimethyl ascorbic acid under similar experimental conditions (Micheel, *Annalen*, 1935, **519**, 70; **525**, 66). This lactone (*isodimethyl gluco-ascorbic acid*) is a structural isomeride of dimethyl gluco-ascorbic acid. It shows no selective absorption and differs in rotation and chemical properties from true dimethyl gluco-ascorbic acid. It has been converted into the latter substance in two ways. In the first, the isomeride is kept for some hours in acetone containing sulphuric acid. Rearrangement of the structure is thereby brought about and crystalline 2 : 3-dimethyl gluco-ascorbic acid is regenerated. This process gives no evidence as to the nature of the change involved, but information on this point is provided by the second mode of transformation. When *iso*dimethyl gluco-ascorbic acid is boiled with methyl-alcoholic hydrogen chloride, a strong absorption band at λ 2400 A. gradually makes its appearance and the product on isolation is a monomethyl gluco-ascorbic acid which does not give a blue colour with ferric chloride. It is not 3-methyl gluco-ascorbic acid (the properties of which are fully described below), but the absorption spectrum and the fact that it reacts smoothly with diazomethane, giving 2 : 3-dimethyl gluco-ascorbic acid, indicate that the ring structure of the ordinary form of gluco-ascorbic acid is present. The substance must, therefore, be *2-methyl gluco-ascorbic acid* (XII). It follows that the methyl group at C_3 is the one involved in the reaction with methyl-alcoholic hydrogen chloride and the series of reactions can best be explained by ascribing the structure (XI) to *iso*dimethyl gluco-ascorbic acid. This differs from (II) in that the hydroxyl group on C_6 has saturated the double bond by the attaching of the hydrogen atom to C_2 and the oxygen to C_3. The methoxyl group at C_3 is then glucosidic in type and its removal during intramolecular rearrangement becomes explicable. This remarkable circumstance leads to the conclusion that the new ring formation is equivalent to the ring closure of a ketose

to give a furanoside. The work of Micheel and our own experiments on dimethyl ascorbic acid show clearly that it is the hydroxyl on C_6 in that substance which is involved in addition at the double bond, and for this reason we have provisionally formulated the second ring in (XI) as five-membered, the ring junctions being at C_3 and C_6. It is possible on stereochemical grounds for a six-membered ring to be formed involving the saturation of the double bond by the primary hydroxyl on C_7, but in view of the close analogy with dimethyl ascorbic acid we are inclined to prefer the structure (XI). An example of this type of isomerisation, which involves simultaneous lactonisation and ring formation by saturation of a double bond, may be held to explain the type of ring closure which occurs when hydrated carlic acid gives rise to carlic acid (Clutterbuck, Raistrick, and Reuter, *Biochem. J.*, 1935, **29**, 871). On this view the formulation of carlic acid would be that shown in (XIV). This structure contains a six-membered ring formed by saturation of the double bond by the hydroxyl group. A possible alternative is given in (XIII), which, however, involves the formation of a seven-membered ring by saturation of the double bond. Clutterbuck, Raistrick, and Reuter (*loc. cit.*) suggested (XIII) as the probable formula for carlic acid, but in view of the work now described it would appear that (XIV) is at least equally probable.



EXPERIMENTAL.

d-*Gluco-ascorbic Acid.*—Imino-*d*-gluco-ascorbic acid was prepared by an improved method from glucosone (compare J., 1934, 1194). Glucosazone (100 g.) was decomposed with concentrated hydrochloric acid (900 c.c.) and filtered from phenylhydrazine hydrochloride. Hydrochloric acid was removed from the filtrate by addition of lead carbonate, and the solution filtered and extracted three times with ether. Potassium cyanide (16 g.) was then added to the clear yellow aqueous solution. The reaction was complete in 1 hour. The solution was centrifuged, exactly neutralised with hydrochloric acid, and concentrated under reduced pressure at 35° to 200 c.c. Crystallisation of the imino-gluco-ascorbic acid was complete in 12 hours; it was filtered off and washed with water, acetone, and ether. Yield, 15—20%. Imino-*d*-gluco-ascorbic acid (6·9 g.), dissolved in *N*-hydrochloric acid (70 c.c.), was kept at room temperature for a week until the absorption band at λ 2750 A. had disappeared and had been replaced by a band at λ 2450 A. Lead acetate solution was added until the reaction to Congo-red was faintly acid. After filtration, dissolved lead was removed as sulphide and the solution was concentrated to 10 c.c. by evaporation at 35° under carbon dioxide (pressure 15 cm.). Some *d*-gluco-ascorbic acid separated (4·8 g.) and the mother-liquors were further concentrated and the residual syrup was dried by distilling through it dry methyl alcohol. The ammonium chloride which separated was filtered off and the solution on evaporation deposited a further

1·4 g. of *d*-gluco-ascorbic acid. This substance after recrystallisation from methyl alcohol, acetone, and light petroleum still contained one molecule of water of crystallisation and had m. p. 140°; $[\alpha]_D^{20°}$ − 22° in water (*c* = 1) (Found: C, 37·2; H, 5·4. Calc. for $C_7H_{10}O_7,H_2O$: C, 37·4; H, 5·4%. 0·052 G. required 5·1 c.c. of *N*/10-iodine when titrated in acid solution). The details of the absorption spectrum and rotatory dispersion have been recorded previously. When the acid was kept in a vacuum desiccator over calcium chloride, the water of crystallisation was slowly given up and the anhydrous substance was obtained.

d-Gluco-ascorbic acid requires one molecular proportion of alkali for neutralisation (100 mg. required 4·45 c.c. of *N*/10-sodium hydroxide. Calc., 4·47 c.c.). The sodium salt had $[\alpha]_D^{20°}$ − 80° in water (*c* = 1·0) (calculated as gluco-ascorbic acid). On acidification, the rotation immediately changes back to − 22°.

d-Gluco-ascorbic acid is oxidised by an aqueous solution of iodine or chlorine (2 atomic proportions: 52 mg. require 5·1 c.c. of *N*/10-iodine), giving a neutral substance (VII) which reacts as a lactone. On titration of the solution containing the oxidation product, two equivalents of alkali are taken up by the hydriodic acid formed during the oxidation, after which the oxidation product takes up one equivalent of alkali slowly and in the manner of a lactone. The primary oxidation product shows no selective absorption, and has $[\alpha]_D$ − 31° (initial value), changing slowly in acid or neutral solution to the equilibrium value $[\alpha]_D$ + 13°. The substance (VII) having $[\alpha]_D$ − 31° can be reduced to *d*-gluco-ascorbic acid by hydrogen sulphide as shown by reappearance of the absorption band and by isolation of the crystalline product, m. p. 138°. After mutarotation has taken place, the acid formed (VIII) is not reducible by hydrogen sulphide to gluco-ascorbic acid. The neutral sodium salt formed from the primary oxidation product has $[\alpha]_D$ + 27° (*c* 1·0, calc. on weight of gluco-ascorbic acid), but on addition of excess of alkali this value rises to + 120° and then rapidly falls (decomposition). The primary oxidation product reduces Fehling's solution readily and is rapidly attacked by permanganate. When oxidised by sodium hypoiodite in alkaline solution, it gives oxalic acid (yield, 80% of the theoretical). The primary oxidation product (both before and after mutarotation has taken place) reacts with phenylhydrazine, giving the yellow substance, m. p. 225° (decomp.) (see J., 1934, 64), which by analogy with the corresponding derivative of *l*-ascorbic acid probably has the structure of a pyrazolone (Ohle, *Ber.*, 1934, **67**, 1750; see *Ann. Reports*, 1934, 182). A red *substance*, m. p. 215°, probably structurally a true osazone, is obtainable from *d*-gluco-ascorbic acid by the action of phenylhydrazine in dilute acetic acid (Found: N, 14·6. $C_{19}H_{20}O_5N_4$ requires N, 14·6%).

l-*Gluco-ascorbic Acid*.—*l*-Gluconolactone was prepared from *l*-arabinose (compare Hudson, Hartley, and Purves, *J. Amer. Chem. Soc.*, 1934, **56**, 1248). The lactone was reduced by sodium amalgam by the standard procedure and the aqueous solution of *l*-glucose so obtained was treated with phenylhydrazine and dilute acetic acid at 70° for 4 hours. *l*-Glucosazone separated and was washed successively with 2% acetic acid, water, benzene, and methylated spirit. The bright yellow crystals obtained had m. p. 206° and were of the high standard of purity required in subsequent operations. *l*-Glucosazone was then converted into *imino*-l-*gluco-ascorbic acid* by the method given above for *d*-glucosazone. Imino-*l*-gluco-ascorbic acid had $[\alpha]_{5780}^{14°}$ + 148° in water (*c*, 1·0); it began to darken at about 215°, and in aqueous solution it showed an intense absorption band at λ 2750 A. (ε, 17,000) (Found: C, 41·0; H, 5·5; N, 6·7. $C_7H_{11}O_6N$ requires C, 40·9; H, 5·4; N, 6·8%). Its chemical properties were identical with those observed for the *d*-enantiomorph and on digestion with *N*-hydrochloric acid at room temperature for 7 days it was quantitatively transformed into *l*-gluco-ascorbic acid (for details of purification, see above), m. p. (hydrate) 140°, $[\alpha]_D^{22°}$ + 24° in water (*c*, 0·7) as hydrate (Found for the anhydrous substance: C, 40·5; H, 4·7. Calc. for $C_7H_{10}O_7$: C, 40·8; H, 4·9%).

3-*Methyl* d-*Gluco-ascorbic Acid*.—*d*-Gluco-ascorbic acid monohydrate (1 g.) was dissolved in dry methyl alcohol (20 c.c.) and titrated with an ethereal solution of diazomethane at − 10°. At first the yellow colour of the diazomethane was discharged immediately, and the reaction was stopped when, after addition of a drop of reagent, the colour persisted for several minutes. Evaporation of the solvent left a colourless syrup, which was dissolved in acetone (10 c.c.) and precipitated by addition of light petroleum. The syrup so obtained slowly crystallised when kept over calcium chloride in a vacuum desiccator. The crystals were triturated with and recrystallised from acetone–light petroleum, giving 3-*methyl* d-*gluco-ascorbic acid*, m. p. 142°, $[\alpha]_D^{20°}$ − 25° in water (*c*, 0·8) (Found: C, 43·2; H, 5·2; OMe, 14·1. $C_8H_{12}O_7$ requires C, 43·4; H, 5·4; OMe, 14·1%). This substance is acid to litmus in aqueous solution (9·0 mg. required 4·0 c.c. of *N*/100-sodium hydroxide for neutralisation. Calc., 4·1 c.c.). It reduces hot Fehling's solution and gives a permanent deep blue-violet colour with aqueous ferric chloride. It reacts

slowly with iodine in acid solution. It shows a strong absorption band at λ 2450 A. (ε, 10,000) in acidified aqueous solution and at λ 2750 A. in dilute alkaline solution. On treatment with diazomethane in methyl-alcoholic solution, it gives quantitatively 2 : 3-dimethyl gluco-ascorbic acid (see below). A small quantity of the crude syrupy monomethyl gluco-ascorbic acid failed to dissolve in acetone. This crystallised slowly and was washed with acetone and dried in a vacuum desiccator. It was acidic, gave no colour with ferric chloride, reduced hot Fehling's solution, did not react with iodine in acidic solution, and had a strong absorption band in acidified aqueous solution at λ 2800 A. and in dilute alkaline solution at λ 3200 A. The yield was insufficient to permit purification, but the substance appeared to have the composition of a monomethyl gluco-ascorbic acid and corresponded in properties to a similar substance obtained by partial methylation of *l*-ascorbic acid (Haworth, Hirst, and Smith, *loc. cit.*).

2 : 3-*Dimethyl Gluco-ascorbic Acid.*—Anhydrous *d*-gluco-ascorbic acid (5 g.) was dissolved in dry methyl alcohol, and dry ether added until a precipitate just began to form. The calculated quantity of diazomethane was then passed into the cooled solution (ice–salt mixture), which was kept overnight in the refrigerator. Next morning the clear yellow solution was evaporated at 35° under diminished pressure to a syrup, which crystallised when rubbed with a little water. The *monohydrate* of 2 : 3-*dimethyl* d-*gluco-ascorbic acid* after recrystallisation from acetone–light petroleum had m. p. 94°, $[\alpha]_D^{20^\circ}$ − 22° in water (*c*, 4·0), − 7° in methyl alcohol (*c*, 0·8). In aqueous solution it showed an intense absorption band with head at λ 2300 A. (ε = 11,000), measurement being made with a solution containing 4 mg. per 100 c.c. (Found : C, 43·0; H, 6·5; OMe, 24·2. $C_8H_{14}O_7,H_2O$ requires C, 42·8; H, 6·4; OMe, 24·6%). Dimethyl gluco-ascorbic acid does not react with acid iodine solution and gives no colour with ferric chloride. It reacts smoothly with sodium hydroxide in aqueous solution, giving a salt which does not display selective absorption. It does not react with methyl-alcoholic ammonia or with liquid ammonia (contrast 2 : 3-dimethyl ascorbic acid).

2 : 3 : 5 : 6 : 7-*Pentamethyl* d-*Gluco-ascorbic Acid.*—Anhydrous dimethyl gluco-ascorbic acid (2 g.) was dissolved in methyl iodide and methyl alcohol and the solution was boiled with silver oxide in the usual way. The syrupy product crystallised, giving 1·5 g. of the fully methylated product. The reaction is, however, sensitive to traces of impurity and frequently little or no methylation can be effected. We have had similar experiences in the methylation of 1 : 3 : 4 : 5-tetra-acetyl fructose, which sometimes is completed in one operation and on other occasions does not take place at all. The factor responsible for stopping the action of the Purdie reagents is at present unrecognised. In the present instance, we found it more satisfactory to proceed as follows. The monohydrate of dimethyl gluco-ascorbic acid (8 g.) was dissolved in methyl alcohol, and the solution evaporated to dryness under reduced pressure. The anhydrous dimethyl gluco-ascorbic acid so obtained was dissolved in dry acetone and treated with methyl iodide and silver oxide in the usual way. The methylation in acetone solution was repeated until the product was completely soluble in methyl iodide (eight treatments). Methylation operations were stopped when the refractive index of the product had become constant at $n_D^{16^\circ}$ 1·4795; on distillation at 150° (bath temp.)/0·04 mm., a colourless syrup was obtained which consisted mainly of *trimethyl gluco-ascorbic acid monoacetone*. This was a colourless syrup soluble in organic solvents but almost insoluble in water, $n_D^{20^\circ}$ 1·4745, $[\alpha]_D^{21^\circ}$ − 1·6° in methyl alcohol (*c*, 4·2). The absorption band in methyl alcohol is at λ 2350 A. (ε, 12,000) (Found : C, 54·3; H, 7·4; OMe, 36·3. $C_{13}H_{20}O_7$ requires C, 54·8; H, 7·4; OMe, 36·3%). The analytical figures indicate slight contamination with pentamethyl gluco-ascorbic acid.

The acetone derivative was hydrolysed by heating with water for 12 hours at 95°. The solution was concentrated under diminished pressure and the syrupy product ($n_D^{22^\circ}$ 1·4925) was methylated six times by silver oxide and methyl iodide. The product ($n_D^{20^\circ}$ 1·4720) crystallised partly * on nucleation with authentic pentamethyl *d*-gluco-ascorbic acid. The solid material was triturated with ether and then recrystallised from ether, giving 2 : 3 : 5 : 6 : 7-*pentamethyl gluco-ascorbic acid*. Yield, 2·5 g. (Found : C, 52·4; H, 7·5; OMe, 56·4. $C_{12}H_{22}O_7$ requires C, 52·2; H, 7·4; OMe 56·2%). M. p. 80°. $[\alpha]_D^{21^\circ}$ − 5° in methyl alcohol (*c*, 1·4); + 21° in carbon tetrachloride (*c*, 3·65). The substance was soluble in the usual organic solvents with the exception of light petroleum, in which it was slightly soluble, and almost insoluble in water. It displayed in methyl-alcoholic solution a strong absorption band with head at λ 2350 A. (ε = 10,000). Pentamethyl gluco-ascorbic acid does not react with *N*/10-sodium hydroxide

* The non-crystalline portion had the composition of a tetramethyl gluco-ascorbic acid, showed zero rotation, did not react with dilute alkali, did not show selective absorption, and could not be further methylated. It did not possess the typical ascorbic acid structure and was not further examined.

in the cold (contrast dimethyl gluco-ascorbic acid) and slowly undergoes profound decomposition when heated with alkali.

Ozonisation of Pentamethyl Gluco-ascorbic Acid.—The acid (1·19 g.) was dissolved in dry freshly distilled carbon tetrachloride (60 c.c.) and a rapid stream of ozonised oxygen was passed through the cooled solution (− 5°) for 4 hours. The rotation changed from $[\alpha]_D^{20°}$ + 21° to − 2·5° (constant value). Water (20 c.c.) was added and the mixture was heated for 30 minutes on the boiling water-bath. The solution was then concentrated under diminished pressure at 30°. The resulting syrup (1·15 g., $n_D^{19°}$ 1·4492) was dissolved in $N/3$-barium hydroxide (50 c.c.) and heated at 60° for 30 minutes, barium oxalate being precipitated. The excess of barium hydroxide was precipitated as the carbonate, and the mixture of oxalate and carbonate was removed by filtration, acidified with sulphuric acid, and titrated with $N/10$-potassium permanganate, 120·1 c.c. being used. This corresponds to a yield of barium oxalate equivalent to 70% of the theoretical value.*

The barium in the clear filtrate was removed by addition of the exact quantity of sulphuric acid. The filtered solution was then concentrated to a syrup, which was boiled with a mixture of ether and chloroform in equal volumes. Evaporation of the solution gave crystalline 3 : 4 : 5-*trimethyl* d-*arabonic acid* in the form of its *monohydrate*, which after recrystallisation from ether had m. p. 67°, $[\alpha]_D^{19°}$ + 5° in methyl alcohol (*c*, 1·0) (Found: OMe, 42·0. $C_8H_{16}O_6,H_2O$ requires OMe, 41·1%). The water of crystallisation was lost slowly when the substance was kept over calcium chloride in a desiccator (Found for the anhydrous substance: C, 46·1; H, 7·8; OMe, 44·3. $C_8H_{16}O_6$ requires C, 46·1; H, 7·8; OMe, 44·7%. 10·2 Mg. required 4·75 c.c. of $N/100$-sodium hydroxide for neutralisation; hence M, 211. Calc. for the anhydrous substance: M, 208).

Methyl 3 : 4 : 5-*trimethyl* d-*arabonate* was formed by boiling the acid (0·54 g.) with methyl-alcoholic hydrogen chloride, isolated in the usual way, and purified by distillation, being obtained as a colourless syrup (0·52 g.), b. p. (bath temp.) 110°/0·03 mm., $n_D^{15°}$ 1·4425, $[\alpha]_{5461}^{16°}$ − 17·5° in methyl alcohol (*c*, 3·1) (Found: C, 48·3; H, 8·1; OMe, 54·2. $C_9H_{18}O_6$ requires C, 48·5; H, 8·2; OMe, 55·8%). Treatment of this ester with methyl-alcoholic ammonia gave the corresponding amide, which crystallised as the *monohydrate*; the latter on recrystallisation from acetone–ether gave long needles, m. p. 51°, $[\alpha]_{5461}^{17°}$ − 30° in water (*c*, 1·0) (Found: C, 42·7; H, 8·9; N, 6·2; OMe, 41·2. $C_8H_{17}O_5N$ requires C, 42·6; H, 8·5; N, 6·2; OMe, 41·3%). This amide gave a strong positive Weerman reaction, the sodium cyanate liberated being recognised after conversion into hydrazodicarbonamide, m. p. 256° alone or on admixture with an authentic specimen (yield, 26 mg. from 25 mg. of the amide). Control experiments with 2 : 3 : 4-trimethyl *l*-arabonamide and 2 : 3 : 5-trimethyl *l*-arabonamide gave no hydrazodicarbonamide.

Anhydrous 3 : 4 : 5-trimethyl arabonic acid was methylated three times by Purdie's reagents. The product was purified by distillation, giving *methyl* 2 : 3 : 4 : 5-*tetramethyl* d-*arabonate*, b. p. 100°/0·1 mm. (bath temp.), $n_D^{16·5°}$ 1·4355 (yield, almost quantitative) (Found: OMe, 62·0. $C_{10}H_{20}O_6$ requires OMe, 65·6%). Treatment of this ester with methyl-alcoholic ammonia gave the corresponding *amide*, which after recrystallisation from ether–light petroleum had m. p. 101°, $[\alpha]_D^{20°}$ + 33° in methyl alcohol (*c* = 1·5; observations taken in a micro-polarimeter tube) (Found: OMe, 55·1. $C_9H_{19}O_5N$ requires OMe, 56·1%). The identity of this substance was confirmed by crystallographic (including *X*-ray) examination and comparison with the corresponding derivative of *l*-arabonic acid. The latter was prepared from calcium *l*-arabonate, which was methylated by methyl sulphate and sodium hydroxide. The product was isolated in the usual way, and methylation completed by use of Purdie's reagents. The fully methylated ester was treated with methyl-alcoholic ammonia, giving 2 : 3 : 4 : 5-*tetramethyl* l-*arabonamide*, m. p. (after recrystallisation from acetone–light petroleum) 101°, $[\alpha]_D^{17°}$ + 34·0° in methyl alcohol (*c*, 1·0) (Found: C, 48·6; H, 9·0; OMe, 56·2. $C_9H_{19}O_5N$ requires C, 48·8; H, 8·9; OMe, 56·1%).

Isomerisation of 2 : 3-*Dimethyl* d-*Gluco-ascorbic Acid.*—This substance reacts in the cold with $N/10$-sodium hydroxide, giving a sodium salt having $[\alpha]_D^{20°}$ + 40° (calc. on concentration of dimethyl gluco-ascorbic acid hydrate), and with $N/10$-barium hydroxide, giving the corresponding barium salt. The sodium salt does not display selective absorption. On addition of excess of mineral acid to the aqueous solution the rotation drops immediately to + 31° and the product does not display selective absorption. The rotation gradually falls to zero (constant

* In other experiments the ozonisation was carried out in glacial acetic acid solution. The product was a neutral ester which on treatment with methyl-alcoholic ammonia gave oxamide (yield, 85% of the theoretical).

value) during 24 hours, and at this stage also no selective absorption is shown. If the solution containing mineral acid is heated at 60°, a weak band develops at λ 2300 A., together with a much stronger band at λ 2800 A. Colorimetric tests then indicate the presence of hydroxymethylfurfuraldehyde and the characteristics of the band at λ 2800 A. are in agreement with the view that it is due to hydroxymethylfurfuraldehyde produced by decomposition. The intensity of the band at λ 2300 A. reaches a maximum corresponding to the presence of a mono- or di-methyl gluco-ascorbic acid equal in amount to some 10% of the weight of dimethyl derivative originally used. On further heating, the band at λ 2300 A. disappears and that at λ 2800 A. reaches an intensity corresponding to nearly complete conversion of dimethyl gluco-ascorbic acid into hydroxymethylfurfuraldehyde.

The substance having zero rotation was isolated as follows: dimethyl gluco-ascorbic acid hydrate (1·4 g.) was dissolved in air-free distilled water (50 c.c.), and a slight excess of barium hydroxide added. After 30 minutes, the excess of barium hydroxide was removed by passing carbon dioxide at 60°. The calculated quantity of sulphuric acid was added to the filtered solution and after separation of barium sulphate in the centrifuge the clear solution was evaporated to dryness under diminished pressure at 40°, leaving a syrup, which was purified by solution in methyl alcohol and removal of the solvent. iso*Dimethyl gluco-ascorbic acid* was then obtained as a colourless glass (1·32 g.), $[\alpha]_D^{20^\circ} \pm 0^\circ$ in water. Its solutions were remarkably transparent to ultra-violet light and did not display selective absorption (tested in concentrated solution) (Found: OMe, 26·3. $C_8H_{14}O_7$ requires OMe, 26·5%). *iso*Dimethyl gluco-ascorbic acid titrates as a lactone and required 1 equiv. of alkali for neutralisation. With methyl-alcoholic ammonia it gave a syrup, which contained combined nitrogen and behaved as an amide, liberating ammonia when heated with dilute alkali (contrast dimethyl gluco-ascorbic acid).

Regeneration of 2 : 3-Dimethyl Gluco-ascorbic Acid from iso*Dimethyl Gluco-ascorbic Acid.*—(a) *Treatment with acetone and sulphuric acid.* To the *iso*-derivative (0·1 g.), dissolved in acetone (100 c.c.), concentrated sulphuric acid (10 c.c.) was carefully added and the solution was left at room temperature for 24 hours. The mineral acid was then neutralised by sodium carbonate and the filtered solution was concentrated to a syrup, which was heated with a little water for 30 minutes. The solution was extracted with ether and then concentrated to a syrup, which was distilled under diminished pressure, b. p. 230°/0·04 mm. (bath temp.). The distillate crystallised on trituration with water, giving the monohydrate of 2 : 3-dimethyl gluco-ascorbic acid, m. p. and mixed m. p. with an authentic specimen, 94°, absorption band in aqueous solution at λ 2300—2350 A. (ε, 11,400). *iso*Dimethyl gluco-ascorbic acid distils unchanged at 230°/0·01 mm. and does not regenerate 2 : 3-dimethyl gluco-ascorbic acid.

(b) *Treatment with methyl-alcoholic hydrogen chloride.* *iso*Dimethyl gluco-ascorbic acid (0·5 g.) was boiled with 3% methyl-alcoholic hydrogen chloride (50 c.c.) for 24 hours. The rotation changed from $[\alpha]_D^{20^\circ} \pm 0^\circ$ to -13° (constant value). The solution darkened in colour; it showed no selective absorption at the beginning of the experiment, but, as the rotation changed, a band developed at λ 2400 A. (in acidified methyl-alcoholic solution) and when the rotation had become constant, its intensity (calc. on the weight of original material used) was ε = 11,000. 43 C.c. of this solution were diluted to 100 c.c. with methyl alcohol and 20 c.c. of this dilute solution (A) were used for titration with silver nitrate (weight of silver chloride obtained was equivalent to 6·6 c.c. of N/10-hydrochloric acid); 50 c.c. of solution were titrated with an ethereal solution of diazomethane (equivalent to 26·2 c.c. of N/10-diazomethane, the ethereal solution of the latter reagent having been standardised against iodine immediately before the experiment). From these figures, it appears that more diazomethane had been used up than would be accounted for by the hydrochloric acid. *iso*Dimethyl gluco-ascorbic acid does not react with diazomethane and it follows that the reaction with methyl-alcoholic hydrogen chloride had resulted in the formation of a substance containing a hydroxyl group capable of reacting with diazomethane (see below). The solution after titration with diazomethane was concentrated under reduced pressure, giving a syrup which slowly crystallised when left in a moist atmosphere. The crystals, after being washed with acetone, had m. p. 94° alone or on admixture with authentic 2 : 3-dimethyl gluco-ascorbic acid monohydrate and in aqueous solution they had an absorption band at λ 2300—2350 A. (ε = 11,000), which disappeared on the addition of alkali.

20 C.c. of the solution (A) (see above) were neutralised with barium carbonate, filtered, and concentrated to a mixture of syrup and solid. The organic material was extracted with acetone, and the acetone solution concentrated to a syrup, which consisted mainly of 2-*monomethyl gluco-ascorbic acid* (Found: OMe, 14·2. $C_8H_{12}O_7$ requires OMe, 14·1%). This gave no colour with ferric chloride (distinction from 3-monomethyl gluco-ascorbic acid), was acidic, and had an

absorption band at λ 2400 A. (ε, 11,000) both in acidified aqueous and in methyl-alcoholic solution, and at about λ 2650 A. (ε, 5000) in dilute alkaline solution. This substance was treated with diazomethane in ethereal solution and after 12 hours the solvent was removed by evaporation, leaving a syrup which slowly crystallised. The solid, after being washed with acetone, had m. p. 94° alone or on admixture with 2 : 3-dimethyl gluco-ascorbic acid hydrate, $[\alpha]_D$ − 7° in methyl alcohol (*c*, 1·0). The absorption spectrum was identical with that of 2 : 3-dimethyl *gluco*-ascorbic acid. The yield of crystalline material (60% of the theoretical) was confirmed in later experiments carried out on a larger scale.

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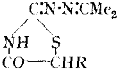
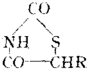
123. *Thiazole and Thiadiazine Formation from Thiosemicarbazones.*

By JOHN MCLEAN and FORSYTH JAMES WILSON.

IT was found by Wilson and Burns (J., 1922, **121**, 870; 1923, **123**, 799) and by Wilson and Stephen (J., 1926, 2531) that thiosemicarbazones in presence of sodium ethoxide reacted with esters of α-halogenated acids to give thiazole derivatives; *e.g.*, CMe_2:N·N:C(SNa)·NH_2 + CHRBr·CO_2Et ⟶ (I) + EtOH + NaBr. Hydrolysis of this thiazole derivative with concentrated hydrochloric acid removed acetone and hydrazine, giving a 2 : 4-diketotetrahydrothiazole (II); 2*N*-hydrochloric acid, however, removed acetone only and the intermediate hydrazone (III) was isolated as the hydrochloride.


(I.)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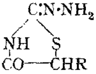
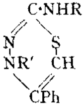
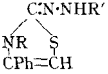
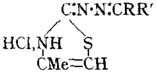

(III.)

Bose and his co-workers (*J. Indian Chem. Soc.*, 1924, **1**, 51; 1925, **2**, 95) have described the reaction of ω-bromoacetophenone with thiosemicarbazide and 4-substituted thiosemicarbazides. From thiosemicarbazide, 2-amino-5-phenyl-1 : 3 : 4-thiadiazine (IV; R = R′ = H) and 2-keto-4-phenyl-2 : 3-dihydro-1 : 3-thiazole-2-hydrazone (V; R = R′ = H) were formed, and substituted thiosemicarbazides produced derivatives of these substances:

NHR·CS·NH·NHR′ + CH_2Br·COPh ⟶ NHR·C(S·CH_2·COPh):N·NHR′ $\xrightarrow{-H_2O}$ (IV) and (V).

(IV.)



(V.)

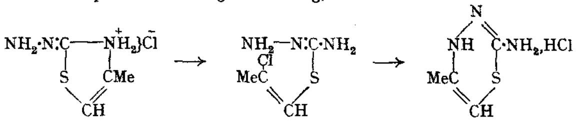

(VI.)

The reactions between chloroacetone and acetonethiosemicarbazone, benzaldehydethiosemicarbazone, and acetophenonethiosemicarbazone, which we have now investigated, conform to the general scheme CRR′:N·N:C(SH)·NH_2 + CH_2Cl·COMe $\xrightarrow{-H_2O}$ (VI), with formation of 2 : 3-dihydrothiazole derivatives. In order to fix the labile hydrogen atom present in the thiosemicarbazone, the sodium derivative was employed and the reactions took a similar course; *e.g.*, with the sodium derivative of acetophenonethiosemicarbazone the reaction produced *2-keto-4-methyl-2 : 3-dihydrothiazole-2-α-phenylethylidenehydrazone.*

Hydrolysis of these 2 : 3-dihydrothiazole derivatives with *N*/10-hydrochloric acid gave the hydrochloride of 2-keto-4-methyl-2 : 3-dihydrothiazole-2-hydrazone (VII), which was exceedingly deliquescent and was identified as the *picrate*. An aqueous solution of the hydrochloride readily formed the corresponding benzylidene and acetophenone derivatives and reduced Fehling's solution immediately in the cold.

Hydrolysis with concentrated hydrochloric acid, however, resulted in the formation the of a six-membered ring, the *hydrochloride* of *2-amino-5-methyl-1 : 3 : 4-thiadiazine* (VIII)

being formed in each case. This enlargement of a five- to a six-membered ring is rather remarkable; we suggest that it may proceed by an opening of the five-ring, followed by reclosure in a new position so as to give a six-ring, thus:



(VII.) (VIII.)

Attempts to prepare the above 1 : 3 : 4-thiadiazine by Bose's method from thiosemicarbazide and chloroacetone in alcoholic solution were not successful, probably because a complex mixture was formed. In concentrated hydrochloric acid solution, however, an excellent yield of 2-amino-5-methyl-1 : 3 : 4-thiadiazine hydrochloride was obtained. Bose (second reference) suggests that thiazole formation from thiosemicarbazides depends on the basic character of the 4-amino-group present in the thiosemicarbazide but that this is not the only factor. The fact that no thiazole is produced when the reaction between thiosemicarbazide and chloroacetone takes place in strongly acid solution would suggest that hydrogen-ion concentration influences the reaction and determines the nature of the product, namely, whether thiazole or thiadiazine will be formed. Some derivatives of 2-amino-5-methyl-1 : 3 : 4-thiadiazine are described.

Chloroacetaldehyde appears to react with thiosemicarbazones in a similar manner to chloroacetone. Reactions were carried out with the thiosemicarbazones of benzaldehyde and acetone, but owing to the small quantity of chloroacetaldehyde available the reaction products were obtained in small quantity and hydrolysis was not attempted.

Experimental.

Chloroacetone and Benzaldehydethiosemicarbazone. Formation of 2-Keto-4-methyl-2 : 3-dihydrothiazole-2-benzylidenehydrazone (VI; R = H, R′ = Ph).—(a) The thiosemicarbazone (8 g.) was dissolved in 100 c.c. of absolute alcohol, 4·5 g. of chloroacetone added, and the mixture refluxed for 15 minutes; a reddish colour developed. After removal of the alcohol under reduced pressure the residue was dissolved in water, and sodium carbonate added. The dark yellow powder which separated was dissolved in dilute hydrochloric acid and reprecipitated with sodium carbonate; the light yellow powder obtained had m. p. 190° after darkening at 185° (Found: N, 19·4; S, 14·7. $C_{11}H_{11}N_3S$ requires N, 19·3; S, 14·7%). The *hydrochloride*, prepared by evaporating a solution of the *substance* in a little *N*/10-hydrochloric acid to dryness under reduced pressure, separated as an almost colourless powder, m. p. 131°, on addition of light petroleum to a chloroform solution (Found: N, 16·6. $C_{11}H_{11}N_3S,HCl$ requires N, 16·7%).

(b) The sodium derivative of benzaldehydethiosemicarbazone separated in theoretical yield when a concentrated absolute-alcoholic solution of the thiosemicarbazone to which sodium (1 atom) had been added was refluxed for ½ hour and then cooled. 10 G. were suspended in chloroform, 5 g. of chloroacetone added, and the liquid refluxed for 10 minutes, filtered from sodium chloride, and concentrated; a substance, m.p. 190°, identical with that described in (a) was obtained.

*Chloroacetone and Acetonethiosemicarbazone. Formation of 2-Keto-4-methyl-2 : 3-dihydrothiazole-2-*iso*propylidenehydrazone* (VI; R = R′ = Me).—A suspension of the thiosemicarbazone (9·8 g.) in about 60 c.c. of chloroform containing 6·9 g. of chloroacetone was refluxed for 10—15 minutes; solution was soon effected. The cold filtered solution was extracted several times with small quantities of water, and neutralisation of the aqueous extract with sodium carbonate precipitated the *substance* as a light yellow powder readily soluble in organic solvents but best purified by solution in acid and precipitation with alkali; it melted at 90° (quickly heated) or 115° (very slowly heated) (Found: N, 25·0; S, 19·0. $C_7H_{11}N_3S$ requires N, 24·8; S, 18·9%).

Chloroacetone and Acetophenonethiosemicarbazone. Formation of 2-Keto-4-methyl-2 : 3-dihydrothiazole-2-α-phenylethylidenehydrazone (VI; R = Ph, R′ = Me).—A hot solution of the thiosemicarbazone (9·6 g.) in benzene was refluxed with 4·6 g. of chloroacetone for 15 minutes. The *hydrochloride* of the substance, which separated during the heating, was recrystallised from

a small quantity of absolute alcohol; it was sparingly soluble in water and melted at 154° (Found: N, 15·6; S, 11·7. $C_{12}H_{13}N_3S,HCl$ requires N, 15·7; S, 11·9%). A warm aqueous solution of the hydrochloride deposited the *substance* itself on addition of sodium carbonate as a cream-coloured powder, which crystallised from aqueous alcohol in colourless prisms, m. p. 134° (Found: N, 18·3. $C_{12}H_{13}N_3S$ requires N, 18·2%).

Formation of 2-Keto-4-methyl-2 : 3-dihydrothiazole-2-α-phenylethylidenehydrazone from Chloroacetone and the Sodium Derivative of Acetophenonethiosemicarbazone.—This sodium derivative was prepared by adding the thiosemicarbazone (1 mol.) to a concentrated solution of sodium ethoxide (1 mol.); solution occurred and after 10 minutes' warming the sodium derivative separated; a further quantity was obtained on addition of light petroleum. It was suspended (9·2 g.) in chloroform, chloroacetone (4 g.) added, and the mixture refluxed for ½ hour. After filtration from sodium chloride, the solution was shaken with a little dilute hydrochloric acid; a hydrochloride identical with the one previously obtained was deposited.

Hydrolysis of the above 2 : 3-Dihydrothiazoles.—In all cases when hydrolysis was effected by boiling with 5*N*-hydrochloric acid two products were obtained, a hygroscopic hydrochloride which could not be obtained pure but could be isolated as the picrate of 2-keto-4-methyl-2 : 3-dihydrothiazole-2-hydrazone, and a hydrochloride identified as the hydrochloride of 2-amino-5-methyl-1 : 3 : 4-thiadiazine. The process may be illustrated by the hydrolysis of 2-keto-4-methyl-2 : 3-dihydrothiazole-2-α-phenylethylidenehydrazone hydrochloride with (a) *N*/10-hydrochloric acid, (b) concentrated hydrochloric acid. (a) The substance (9 g.) with 40 c.c. of acid was steam-distilled till no more acetophenone passed over (¾ hour). The residual solution on evaporation under reduced pressure gave a deliquescent hydrochloride. Addition of picric acid to the aqueous solution gave *2-keto-4-methyl-2 : 3-dihydrothiazole-2-hydrazone picrate*, which separated from boiling water as a yellow microcrystalline powder, m. p. 192° (Found: N, 23·6. $C_4H_7N_3S,C_6H_3O_7N_3$ requires N, 23·4%).

(b) The liquid obtained by heating the substance with acid for 10 minutes under reflux was steam-distilled to remove acetophenone and evaporated to dryness under reduced pressure. The residual *2-amino-5-methyl-1 : 3 : 4-thiadiazine hydrochloride* was washed with cold absolute alcohol; it crystallised, though with difficulty, from this boiling solvent in colourless prisms, m. p. 228° (Found: N, 25·6. $C_4H_7N_3S,HCl$ requires N, 25·4%). It did not reduce Fehling's solution in the cold and did not react with benzaldehyde (absence of hydrazino-group). The *picrolonate* of the base, deposited on addition of aqueous-alcoholic picrolonic acid to an aqueous solution of the hydrochloride, crystallised from dilute alcohol in golden-yellow needles, m. p. 235° (Found: N, 25·0. $C_4H_7N_3S,C_{10}H_8O_5N_4$ requires N, 24·9%).

2-Amino-5-methyl-1 : 3 : 4-thiadiazine was synthesised by heating on the water-bath a suspension of thiosemicarbazide (4 g.) in about 40 c.c. of concentrated hydrochloric acid with chloroacetone (4·3 g.). On standing over-night, colourless prisms of a hydrochloride, m. p. 228°, identical with the previous specimen, were deposited (picrolonate, m. p. 235°); a further quantity was obtained by concentration. An aqueous solution of the salt to which the requisite quantity of potassium hydroxide had been added was evaporared to dryness, and the residue extracted with hot benzene (charcoal), from which, on cooling, the base separated in cream-coloured prisms, m. p. 109° (Found: N, 32·7. $C_4H_7N_3S$ requires N, 32·7%). It was not stable, undergoing rapid oxidation in the air. The base dissolved in acetic anhydride with evolution of heat; on standing, the *triacetyl* derivative was deposited in plates, which could be recrystallised from benzene–light petroleum; m. p. 167° (Found: C, 47·1; H, 5·1; N, 16·4. $C_{10}H_{13}O_3N_3S$ requires C, 47·1; H, 5·1; N, 16·5%). The *dibenzoyl* derivative was obtained by treating the base with benzoyl chloride and after some time shaking the resultant oil with sodium carbonate; the crystals so obtained could be purified from alcohol and melted at 201—202° (Found: N, 12·5. $C_{18}H_{15}O_2N_3S$ requires N, 12·5%).

Owing to the presence of the amino-group the base reacted with carbon disulphide and with phenylthiocarbimide as described below.

2-Amino-5-methyl-1 : 3 : 4-thiadiazine 5-methyl-1 : 3 : 4-thiadiazine-2-dithiocarbamate, $C_4H_7N_3S,HS{\cdot}CS{\cdot}NH{\cdot}C{<}{\begin{matrix}N{\cdot}NH\\S{-}CH\end{matrix}}{>}CMe$, was prepared by warming 4 g. of the thiadiazine base in alcoholic solution containing about 2 g. of potassium hydroxide and 6 g. of carbon disulphide. The liquid soon solidified to a mass of yellow crystals which, after washing with water and alcohol, decomposed at 142° (Found: N, 25·3. $C_4H_7N_3S,C_5H_7N_3S_2$ requires N, 25·4%).

2-Anilinothioformamido-5-methyl-1 : 3 : 4-thiadiazine was prepared by adding 4·1 g. of phenylthiocarbimide to a suspension of 3·8 g. of the thiadiazine base in about 30 c.c. of benzene; the suspension became warm and soon solidified. After collection and washing with benzene the

thiourea crystallised from absolute alcohol in minute colourless needles, m. p. 200° (decomp.) (Found : N, 21·2. $C_{11}H_{12}N_4S_2$ requires N, 21·2%).

Chloroacetaldehyde and Acetonethiosemicarbazone. Formation of 2-Keto-2 : 3-dihydrothiazole-2-isopropylidenehydrazone (VI; R = R′ = Me, Me at 4 = H).—A solution of the thiosemicarbazone (2 g.) in 20 c.c. of absolute alcohol containing 1 g. of chloroacetaldehyde was refluxed for 10 minutes, cooled, diluted to 100 c.c. with water, and treated with dilute sodium carbonate solution till just alkaline. The yellow precipitate, dissolved in dilute hydrochloric acid and reprecipitated with sodium carbonate, gave a cream-coloured powder, m. p. 140° (Found : N, 27·1. $C_6H_9N_3S$ requires N, 27·1%), readily soluble in organic solvents and crystallisable from aqueous alcohol.

Chloroacetaldehyde and Benzaldehydethiosemicarbazone. Formation of 2-Keto-2 : 3-dihydrothiazole-2-benzylidenehydrazone (VI; R = H, R′ = Ph, Me at 4 = H). The thiosemicarbazone (1·8 g.) with 0·8 g. of chloroacetaldehyde in absolute alcohol was refluxed for ½ hour, and the solution concentrated to small bulk, considerably diluted with water, and neutralised with sodium carbonate. The solid deposited after standing and scratching was dissolved in dilute hydrochloric acid, reprecipitated with sodium carbonate, and obtained as a cream-coloured powder, m. p. 169° (Found : N, 20·6. $C_{10}H_9N_3S$ requires N, 20·7%).

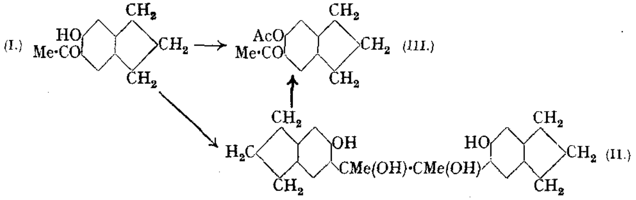
We wish to thank Imperial Chemical Industries, Ltd., for a research grant.

"Freeland" Chemical Laboratories,
The Royal Technical College, Glasgow. [*Received, January 28th*, 1937.]

124. *Pinacols Derived from* o-*Hydroxyacetophenones.*

By Wilson Baker and J. C. McGowan.

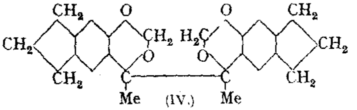
Mention has been made of the fact that 5-hydroxy-6-acetylhydrindene (I) in sodium hydroxide solution is reduced by zinc dust to one of the two possible inactive forms of the corresponding pinacol, 6-(*5-hydroxyhydrindyl*)*methylpinacol* (II), but that the isomeric 5-hydroxy-4-acetylhydrindene, in which the acetyl group may be regarded as sterically hindered by the adjacent methylene group, is unaffected under these conditions (Baker, this vol., p. 476).

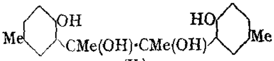


The structure assigned to (II) was based on the following facts : (1) the elementary analysis; (2) it gave no yellow, sparingly soluble sodium salt, as do *o*-hydroxyacetophenones; (3) its alcoholic solution gave an intense blue coloration with ferric chloride, a reaction exhibited by *o*-hydroxybenzyl alcohol and derivatives; (4) its physical properties were not in harmony with those which might be expected of the corresponding secondary alcohol. Molecular-weight determinatons of (II) in camphor gave the low value of 192 (II requires *M*, 354; the secondary alcohol directly derived from I requires *M*, 178), but this result was almost certainly due either to dismutation into (I) and the corresponding secondary alcohol, or to formation of (I) owing to oxidation by the camphor. That such an explanation was probable followed from the observation that with boiling acetic anhydride (II) was converted apparently quantitatively into *5-acetoxy-6-acetylhydrindene* (III), identical with the compound prepared similarly from (I). Molecular-weight determinations

of (II) by the cryoscopic method were impossible owing to the sparing solubility of the substance, and ebullioscopic methods were worthless owing to its instability.

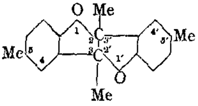
Direct confirmation of the correctness of formula (II) has now been obtained. When treated in dilute acetone solution with sodium hydroxide and methylene sulphate (compare the methylenation of *o*-hydroxybenzyl alcohol; Baker, J., 1931, 1765), the compound yields its dimethylene ether, 4 : 4'-*bis*-(4-*methyl*-6 : 7-*trimethylene*-1 : 3-*benzdioxinyl*) (IV), whose molecular weight indicates the formula given. A further study of these reactions was undertaken in the case of a more accessible *o*-hydroxyacetophenone, namely,

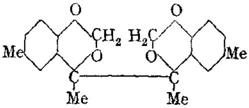

(IV.)


(V.)

3-acetyl-*p*-cresol. The reaction in this case leads to the production of the two stereoisomeric pinacols, 4-*hydroxy*-m-*tolylmethylpinacols* (V), in a total yield of over 80%. The more readily isolable stereoisomer, produced in some 20% yield, has the higher melting point, and will be referred to as the α-pinacol. The lower-melting β-pinacol is produced in 60% yield. It was not found possible to determine the molecular weights of either of these pinacols owing to their reactive nature; the α-pinacol is insufficiently soluble in cold organic solvents and is insufficiently stable in hot solvents. Thus, on heating for a short time with acetic acid, it is converted into one (α-form) of the two possible stereoisomeric forms of the alkali-insoluble 2 : 3 : 5 : 5'-*tetramethylcoumarano*-3' : 2' : 2 : 3-*coumaran* (VI). The β-pinacol, on the other hand, is not so readily cyclised; when heated in alcohol with a trace of concentrated hydrochloric acid, or with a solution of sodium acetate in acetic acid, it gives what appears to be a mixture of (VI) and possibly a higher-melting stereoisomer. On the other hand it appears to undergo dismutation on heating in neutral solvents. Thus it cannot be satisfactorily recrystallised from carbon tetrachloride, and 3-acetyl-*p*-cresol may be detected in the mother-liquors.

Each pinacol (V), when treated in dilute acetone solution with sodium hydroxide and methylene sulphate, gives a distinct dimethylene ether; the substances are the stereoisomeric forms of 4 : 4'-*bis*-(4 : 6-*dimethyl*-1 : 3-*benzdioxinyl*) (VII).

(VI.) 

 (VII.)

There is no conclusive evidence as to which of the two isomeric pinacols (V) is the racemic and which the *meso*-form. On the probable assumption, however, that the more readily produced 2 : 3 : 5 : 5'-tetramethylcoumarano-3' : 2' : 2 : 3-coumaran (VI), m. p. 151°, has the two five-membered rings fused in the *cis*-position, the α-pinacol, from which (VI) is smoothly prepared, should be the racemic form, the β-pinacol being consequently the *meso*-form. The argument can, of course, be extended to the two stereoisomeric 4 : 4'-bis-(4 : 6-dimethyl-1 : 3-benzdioxinyl)s (VII), of which the α-isomer is most probably the racemic form, and the β-isomer the *meso*-form.

Most of the above reactions have parallels in the literature. The dismutation of pinacols was probably first observed by Linnemann (*Annalen*, 1865, **133**, 1), the correct interpretation of the reaction being given by Thörner and Zincke (*Ber.*, 1877, **10**, 1473); Cohen (*Rec. trav. chim.*, 1919, **38**, 113) showed that benzophenone pinacols undergo dismutation in presence of alkali; Shoppee (J., 1936, 506) has recently shown that *s*-di-*p*-anisylpinacol undergoes complete dismutation on melting. Coumarano-3' : 2' : 2 : 3-coumarans of the type (VI) have been prepared in stereoisomeric forms by the reduction of salicylaldehyde (Tiemann, *Ber.*, 1891, **24**, 3171; Harries, *ibid.*, p. 3175), 2-hydroxy-5-

methylbenzaldehyde (Anselmino, *Ber.*, 1908, **41**, 621), and 2-hydroxy-1-naphthaldehyde (Betti and Mundici, *Gazzetta*, 1906, **36**, ii, 656) with zinc dust and acetic acid, but do not appear to have been previously prepared from the pinacols which must be regarded as intermediates. The ease with which the pinacols undergo this type of ring closure is their most remarkable feature.

Experimental.

6-(5-*Hydroxyhydrindyl*)*methylpinacol* (II).—A mixture of 5-hydroxy-6-acetylhydrindene (I) (2 g.) (Baker, *loc. cit.*) in 4% aqueous sodium hydroxide (50 c.c.) and zinc dust (20 g.) was heated on the water-bath for 6 hours with occasional shaking, then filtered, and the remaining zinc washed with a little dilute sodium hydroxide solution. The combined filtrates were acidified; the solid obtained crystallised from 50% alcohol (50 c.c.) in colourless rectangular plates (1 g.), m. p. 122° (Found: C, 74·8; H, 7·3. $C_{22}H_{26}O_4$ requires C, 74·6; H, 7·3%). The *pinacol* is difficult to crystallise and there is always appreciable loss, probably due to dismutation. It is soluble in dilute aqueous sodium hydroxide with a very pale yellow colour, and its alcoholic solution gives an intense blue ferric chloride coloration, which becomes violet on the addition of water. The solution in concentrated sulphuric acid is yellow.

5-*Acetoxy*-6-*acetylhydrindene* (III).—(a) 5-Hydroxy-6-acetylhydrindene (1 g.) was refluxed for 4 hours with acetic anhydride (10 c.c.), the solution shaken with water, and the solid collected and recrystallised from light petroleum (b. p. 60—80°). The *product* formed stout diamond-shaped plates, m. p. 88° (Found: C, 71·4; H, 6·9; *M*, 210. $C_{13}H_{14}O_3$ requires C, 71·5; H, 6·4%; *M*, 218). (b) An exactly similar experiment with the pinacol (II) gave a product melting at 88° either alone or when mixed with the acetate prepared as in (a). Hydrolysis of this acetate with dilute alcoholic sodium hydroxide readily gave 5-hydroxy-6-acetylhydrindene, m. p. 59°.

4 : 4′-*Bis*-(4-*methyl*-6 : 7-*trimethylene*-1 : 3-*benzdioxinyl*) (IV).—A solution of 6-(5-hydroxyhydrindyl)methylpinacol in dilute acetone was treated with 10% aqueous potassium hydroxide, and methylene sulphate added in small portions at a time with shaking and warming. The solid alkali-insoluble *ether* (IV) was collected, washed, and crystallised twice from ethyl alcohol. It formed fern-like aggregates of prisms, m. p. 172° (Found: C, 75·6; H, 6·5; *M*, 335. $C_{24}H_{26}O_4$ requires C, 76·1; H, 6·9%; *M*, 378). The substance dissolves in concentrated sulphuric acid with a bright orange colour.

Stereoisomeric Forms of 4-*Hydroxy*-m-*tolylmethylpinacol* (V).—The following method of reduction and isolation of the products was adopted as the result of a large number of experiments. 3-Acetyl-*p*-cresol (40 g.; see Baker, J., 1933, 1388), sodium hydroxide (40 g.), water (1000 c.c.), and zinc dust (200 g.) were heated together on the water-bath for 10 hours with continuous mechanical stirring. The cooled solution was filtered from the excess of zinc and made faintly acid to litmus by the addition of 20% acetic acid, and the precipitated solid was collected after standing overnight, washed with dilute acetic acid, and dried at room temperature. It was now digested with boiling absolute alcohol for 1 hour and, after cooling, the residual solid, the α-*pinacol*, was collected by filtration, the β-*pinacol* remaining in the alcoholic solution.

The α-pinacol (yield, 8 g.) is best recrystallised from alcohol, in which it is very sparingly soluble, by continuously extracting the solid in a Soxhlet apparatus, and separates in minute, almost rectangular plates, which melt with evolution of gas at about 273° when rapidly heated (Found: C, 71·4; H, 7·5. $C_{18}H_{22}O_4$ requires C, 71·5; H, 7·3%). The substance is difficultly soluble in all ordinary organic solvents.

The β-pinacol was obtained from the alcoholic solution (above) by evaporation to a syrup; it solidified on cooling. The yield after complete removal of the alcohol was 24·5 g. It was crystallised twice from ethyl acetate and obtained as a microcrystalline powder melting with decomposition at about 170° (Found: C, 71·5; H, 7·3. $C_{18}H_{22}O_4$ requires C, 71·5; H, 7·3%).

Both the α- and the β-pinacol give colourless solutions in aqueous sodium hydroxide and orange solutions in concentrated sulphuric acid, reduce Fehling's solution and ammoniacal silver nitrate, and give brilliant blue solutions with alcoholic ferric chloride.

α-2 : 3 : 5 : 5′-*Tetramethylcoumarano*-3′ : 2′ : 2 : 3-*coumaran* (VI).—The α-pinacol (V) was dissolved in boiling glacial acetic acid; on standing, a small quantity of the original pinacol separated. The filtered solution was concentrated and poured into water, and the solid product collected, washed with dilute aqueous sodium hydroxide, and recrystallised twice from alcohol. It formed flat prisms, m. p. 151° (Found: C, 81·1; H, 6·7; *M*, 268. $C_{18}H_{18}O_2$ requires C, 81·2; H, 6·7%; *M*, 268), insoluble in boiling sodium hydroxide solution, and gave no ferric

chloride reaction in alcoholic solution. Its solution in concentrated sulphuric acid is intensely orange.

Ring Closure of the β-Pinacol.—(a) The β-pinacol was boiled for a few minutes in alcoholic solution containing a few drops of concentrated hydrochloric acid. The material which separated on cooling was washed with sodium hydroxide solution and recrystallised three times from alcohol; it formed a powder, m. p. 150—183° (Found: C, 79·0; H, 6·7%). (b) The β-pinacol (4 g.), acetic acid (30 c.c.), and anhydrous sodium acetate (3 g.) were refluxed for 6 hours. The cooled solution was treated with an excess of dilute aqueous sodium hydroxide, and the solid collected, washed, and recrystallised from alcohol. The product had m. p. 150—164°, and a mixture with the product (VI), m. p. 151°, derived from the α-pinacol, melted over the range 150—156°.

Methylenation of the Pinacols (V).—(a) The α-pinacol (5 g.) and sodium hydroxide (8 g.) were treated with sufficient dilute acetone (40%) to give a homogeneous solution. Methylene sulphate (9 g.) was now added, and the mixture warmed on the water-bath for ½ hour. After removal of the acetone, the solid was collected, washed, dried, and extracted with light petroleum in a Soxhlet apparatus. The *α-4 : 4′-bis-(4 : 6-dimethyl-1 : 3-benzdioxinyl)* which separated from the petroleum was crystallised twice from benzene and obtained in microscopic prisms, m. p. 243° (Found: C, 73·4; H, 6·8; *M*, 331. $C_{22}H_{22}O_4$ requires C, 73·6; H, 6·7%; *M*, 326). The yield was poor.

(b) The β-pinacol was methylenated in exactly the same way. The crude product was precipitated in good yield by the addition of water, collected, washed with dilute sodium hydroxide solution, and crystallised twice from alcohol. The *β-4 : 4′-bis-(4 : 6-dimethyl-1 : 3-benzdioxinyl)* was obtained as microscopic plates, m. p. 134—135° (Found: C, 73·6; H, 6·7; *M*, 317. $C_{22}H_{22}O_4$ requires C, 73·6; H, 6·7%; *M*, 326). Its solution in concentrated sulphuric acid is deep red.

THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, February 1st, 1937.*]

125. *Anthelmintics: Kousso. Part I. Protokosin.*

By B. A. HEMS and A. R. TODD.

THE dried female flowers of *Hagenia abyssinica* (= *Brayera anthelmintica*) have long been used as an anthelminthic drug under the name "kousso" or "koso," particularly in North Africa and the Near East; in Europe it has been largely displaced by extracts of the male fern (*Filix mas*). Investigations of kousso were made by numerous workers from 1839 onwards, but the early literature is in a very confused state; a useful summary of the early work is given by Kondakow (*Arch. Pharm.*, 1899, **237**, 481). The first definite crystalline product from kousso appears to have been the *kosin*, m. p. 142°, prepared by Messrs. E. Merck by an extraction process involving treatment of the flowers with hot milk of lime and subsequent extraction with alcohol. This preparation was investigated by Flückiger and Buri (*Arch. Pharm.*, 1874, **5**, 205), who ascribed to it a formula $C_{31}H_{38}O_{10}$. Leichsenring (*ibid.*, 1894, **232**, 50) isolated from an ethereal extract of kousso, protokosin, a colourless crystalline compound with no vermicidal properties, and kosotoxin, an amorphous, highly toxic substance: to them he allotted the formulæ $C_{29}H_{38}O_9$ and $C_{26}H_{34}O_{10}$ respectively. By treatment of protokosin with hot baryta he obtained a product identical with Merck's kosin, for which he proposed a formula $C_{23}H_{30}O_7$. Lobeck (*Arch. Pharm.*, 1901, **239**, 672), using a modified form of the old alkaline extraction process, isolated kosin together with small quantities of protokosin and a third substance, kosidin, having very similar properties. His analytical data for kosin and protokosin agreed with those of Leichsenring (*loc. cit.*), but he was able to show that the so-called kosin was really a mixture of two isomers, α- and β-kosin. Apart from the fact that both kosin and kosotoxin gave on akali fusion *iso*butyric acid and traces of substances resembling phloroglucinol derivatives, nothing further appears to be known regarding the nature of any of the above substances.

From an ethereal extract of kousso we have isolated, in a yield of 0·4% and by a much simpler process than that of Leichsenring (*loc. cit.*), a substance having the recorded properties of protokosin. A search was made for Lobeck's kosidin, but none could be isolated;

from his description of its preparation and properties we are of the opinion that his product was mainly impure protokosin. The amorphous material to which Leichsenring gave the name kosotoxin was also obtained, but has not yet been thoroughly investigated.

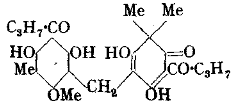
Analysis and molecular-weight determinations indicate for protokosin a formula $C_{22}H_{28}O_7$ rather than that proposed by Leichsenring (*loc. cit.*); it contains one methoxy-group, and side-chain methyl estimations (Kuhn–Roth) indicate the probable presence of four CH_3·C groups. Protokosin has phenolic properties, but, like earlier workers, we are unable to prepare any crystalline derivatives, though an amorphous acetate which seemed to contain three acetyl groups was obtained; in solution it is dextrorotatory. Alkaline degradation of protokosin was found to be more satisfactory with sodium hydroxide than with barium hydroxide which was used by Leichsenring; on heating for 5 minutes with 20% aqueous sodium hydroxide in presence of zinc dust it yielded a fatty acid, and two other crystalline products, one lemon-yellow and one colourless.

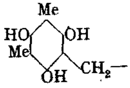
The colourless product was identified by comparison with synthetic material as *C*-trimethylphloroglucinol and the relatively mild conditions of reaction justify the assumption that in its formation no demethylation has occurred. The pale yellow product was identical with Merck's kosin, of which a small sample was available for comparison through the kindness of Messrs. E. Merck, Darmstadt, to whom our thanks are due. By fractional crystallisation we were able to separate this material into two distinct compounds, α-kosin, m. p. 158° (yellow needles), and β-kosin, m. p. 120° (yellow prisms), the former being present in much larger quantity; these compounds are presumably identical with those obtained by Lobeck (*loc. cit.*) from Merck's kosin. Analysis and molecular-weight determinations showed that α- and β-kosin are isomeric with each other and with protokosin; they differ from the latter compound (1MeO) in that both contain two methoxy-groups and they are optically inactive. They are phenolic in nature, and form crystalline triacetyl derivatives. Accurate methoxyl determination is difficult with these compounds, repeated analyses failing to give satisfactory values; this difficulty has also been encountered by Boehm in his studies of compounds from *Aspidium filix mas* (cf. *Annalen*, 1901, **318**, 230). α- and β-Kosin are very resistant to further breakdown by alkali; after boiling even with 80% sodium hydroxide, most of the starting material was recovered unchanged; from the part attacked, no identifiable products could be isolated.

The fatty acid obtained in the alkaline treatment of protokosin is also produced by the action of sulphuric acid, and was reported by Leichsenring, on scanty evidence, to be *iso*butyric acid. This we have confirmed, the acid being identified as its *p*-phenylphenacyl ester and its *p*-toluidide. The amount of *iso*butyric acid liberated on heating protokosin with sulphuric acid at 160°, or with alkali at 100°, was determined; the figure obtained corresponded approximately to the presence of one *iso*butyryl group in the original substance.

When fused with alkali, protokosin gave, in addition to amorphous products, a small yield of a crystalline substance, identified as *C*-monomethylphloroglucinol by comparison with a synthetic specimen. A variety of oxidative and other degradations were carried out on protokosin, but all gave negative results.

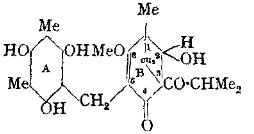
The properties and reactions of protokosin are reminiscent of those shown by compounds isolated from the anthelmintic *Aspidium filix mas* (cf. Boehm, *loc. cit.*). The remarkable conversion of protokosin into α- and β-kosin under the influence of alkali has a parallel in the behaviour of aspidin (I), which under similar conditions yields an isomeric yellow alkali-stable compound containing an additional methoxy-group (Boehm, *Annalen*, 1903, **329**, 321). The mechanism of this reaction is not clear; it apparently involves the migration of a methyl group from carbon to oxygen. Furthermore many compounds of the *Aspidium filix mas* group contain a butyryl group removable by acid or alkali, and give phloroglucinol derivatives on alkali treatment.

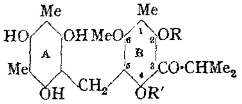
(I.) 

 (II.)

It seems reasonable to assume that protokosin is somewhat similarly constituted to the *Aspidum filix mas* products, *i.e.*, that it is a derivative of methylenebisphloroglucinol.

The isolation of *C*-trimethylphloroglucinol as described above fixes for one ring the structure (II); for the remainder of the molecule the evidence is not decisive, but sufficient is available to permit of a suggestion as to its probable nature. This portion of the molecule must accommodate the methoxy-group and the *iso*butyryl side chain, and at the same time explain its optical activity and allow for the conversion into the isomeric inactive α- and β-kosins, which are both phenolic and more stable than protokosin. A possible formula for protokosin which fulfils these requirements is (III); a definite formula can only be assigned to it when further evidence becomes available.

(III.) 

 (IV.)

The methylene bridge in ring B is preferred to a *gem*-dimethyl group, since oxidation of protokosin, by the method employed by Boehm (*Annalen*, 1901, **318**, 230) in the case of filix acid, yielded no *gem*-dimethylphloroglucinol derivatives, nor could dimethylmalonic acid be obtained by potassium permanganate oxidation under conditions known to permit of its isolation. Protokosin does not react with the usual carbonyl reagents, possibly for steric reasons, and it gives no condensation product with diazoaminobenzene; the latter fact indicates that, if it is a methylenebisphloroglucinol derivative, it bears a methoxy-group in an ortho-position to the point of attachment of the methylene bridge between the two nuclei and contains no free methin group (Boehm, *Annalen*, 1903, **329**, 269). The position of the methoxy-group also explains the failure to obtain a xanthene derivative on warming with a solution of hydriodic acid in glacial acetic acid.

On the basis of formula (III) the two kosins could be represented by (IV; R = H; R′ = Me) and (IV; R = Me; R′ = H), the position of the second methoxy-group being deduced as follows. Protokosin apparently yields only a triacetate, and it seems most likely on steric grounds that the hydroxyl in position 2 is the one unaffected by acetylation. Analogies are found for this in *Aspidium filix mas* products, *e.g.*, aspidin (I) gives only a di- and not a tetra-acetate (Boehm, *loc. cit.*). Both α- and β-kosin also give triacetates. It is clear that when ring B in protokosin is aromaticised by rupture of the bridge between C_1 and C_3 a new hydroxy-group appears at C_4; this should offer the same resistance to acylation as the C_2 hydroxyl, the steric hindrance being similar in both cases. If, then, the new methoxy-group in each of the kosins is situated in ring B, on acetylating them only the three hydroxyls in ring A will be affected; it is difficult to find any other formulation which explains the production of triacetates.

It is not possible to draw any conclusions from the production of *C*-monomethylphloroglucinol on fusing protokosin with alkali, since the treatment was so drastic that its formation by further degradation of *C*-trimethylphloroglucinol cannot be excluded.

Experimental.

Isolation of Protokosin.—Dried commercial kousso (25 kg.) was exhaustively extracted with ether by percolation at room temperature, and the extract concentrated to a dark green syrup (*ca.* 2·5 l.). This syrup was extracted in portions of 500 g. with boiling light petroleum (2 l., b. p. 40—60°), and the extracts decanted off and evaporated. The residue, dissolved in hot alcohol (1 l.) and allowed to stand for 2 days, deposited a considerable amount of waxy material, which was filtered off; after concentration to about 300 c.c. the filtrate slowly deposited *protokosin*, which was collected at intervals of 2—3 days during 2 weeks. On prolonged standing, further small amounts of the same product separated. Total yield, 100 g.; m. p. 179°.

The crude product, which had a slightly greenish colour, crystallised from chloroform–

alcohol in colourless needles, m. p. 182°, not raised by further crystallisation [Found : C, 65·4, 65·2, 65·4; H, 7·0, 7·0, 7·0; MeO, 8·1, 8·0, 8·1; *M* (Rast), 412, 396, 399. $C_{21}H_{23}O_{6}(OMe)$ requires C, 65·4; H, 6·9; MeO, 7·6%; *M*, 404].

Oxidation with chromic acid (Kuhn–Roth) gave 3·0, 3·3 mols. of acetic acid, corresponding to the presence of four side-chain methyl groups. Hydroxyl estimations (Zerewitinoff) gave 11·6, 11·7% OH (calc. for three OH, 12·6%) (cf. α- and β-kosin below).

Protokosin has the properties given by Leichsenring (*loc. cit.*). It is insoluble in water, dissolves with difficulty in alcohol and light petroleum, and is readily soluble in ether, acetone, ethyl acetate, and chloroform. It is insoluble in cold sodium carbonate solution, but dissolves slowly in sodium hydroxide to a yellow solution. Its solution in concentrated sulphuric acid, at first pale green, becomes deep red on warming, and alcoholic solutions give with ferric chloride a red-brown colour. It decolorises potassium permanganate rather slowly and does not react with 2 : 4-dinitrophenylhydrazine. In chloroform solution (*c*, 10%) it has $[\alpha]_D + 8·0°$. No crystalline acyl or methoxy-derivatives could be prepared. No xanthene derivative was formed on heating with a solution of hydriodic acid in acetic acid.

Acetylation of Protokosin.—Protokosin (500 mg.) was dissolved in pyridine (5 c.c.), and acetic anhydride (5 c.c.) added; after standing in the cold for 36 hours, the solution was poured into water. A friable solid separated, m. p. 90—100°. It could not be purified (Found by hydrolysis with hot 2% potassium hydroxide : $CH_3·CO$, 22·4. Calc. for a triacetate : $CH_3·CO$, 23·8%).

Kosidin and Kosotoxin.—Efforts to isolate kosidin (Lobeck, *loc. cit.*) from the light petroleum insoluble fraction of the kousso extract were unsuccessful; no evidence for the presence of any crystalline material other than a little protokosin could be obtained. In view of this result and of the close similarity between the recorded properties of kosidin and protokosin, we incline to the view that the so-called kosidin of Lobeck was simply impure protokosin. The kosotoxin obtained from the alcoholic mother-liquors in the extraction process has not yet been submitted to detailed investigation.

Alkali Treatment of Protokosin.—A mixture of protokosin (20 g.), zinc dust (10 g.), and aqueous sodium hydroxide (200 c.c. of 20%) was heated to boiling for 5 minutes, cooled, and filtered from zinc. The yellow filtrate was acidified and extracted several times with ether, the extract being washed with sodium bicarbonate solution. After drying over sodium sulphate, the combined ethereal extracts were evaporated, and the residue dissolved in a small amount of methyl alcohol. On cooling to − 15°, " kosin " (*ca.* 6 g.) separated.

After separation of the kosin, the solution was evaporated, and the residue boiled with benzene until the insoluble portion became powdery; the insoluble material crystallised from water in colourless needles (1·5 g.), m. p. 184° (Found : C, 64·8; H, 7·0. Calc. for $C_9H_{12}O_3$: C, 64·3; H, 7·1%). That this product is *C*-trimethylphloroglucinol was established by comparison with a specimen of that substance (m. p. 184°) prepared by the method of Weidel (*Monatsh.*, 1898, **19**, 250); the reactions were identical and a mixed m. p. showed no depression.

The sodium bicarbonate washings from the above experiment were acidified, combined with the original aqueous acid liquors, and steam-distilled. The distillate, which smelt strongly of *iso*butyric acid, was extracted with ether, the extract dried, and the ether distilled off. From the acidic residue the *p*-phenylphenacyl ester was prepared by the method of Drake and Bronitsky (*J. Amer. Chem. Soc.*, 1930, **52**, 3715); it had m. p. 72°, not depressed by the ester (m. p. 72°) prepared from authentic *iso*butyric acid. For further confirmation a *p*-toluidide was prepared. Recrystallised from light petroleum, this had m. p. 104°, alone or mixed with *iso*butyro-*p*-toluidide (m. p. 104°). No trace of *n*-butyric or other acids was detected.

Fractionation of Kosin.—Repeated crystallisation of crude kosin (6 g.) from methyl alcohol yielded two yellow substances, the less soluble α-kosin (*ca.* 4·5 g.) crystallising in needles and the much more soluble β-kosin (*ca.* 1 g.) forming prisms.

α-Kosin forms pale yellow needles, m. p. 158°, when pure; the ordinary product has m. p. 152°, which can only be further raised with great difficulty [Found : C, 65·3, 65·1; H, 7·0, 6·8; MeO, 13·5, 13·2; *M*(Rast), 393. $C_{20}H_{22}O_5(OMe)_2$ requires C, 65·4; H, 6·9; MeO, 15·3%; *M*, 404]. α-Kosin is optically inactive. Hydroxyl determinations (Zerewitinoff) gave rather unsatisfactory values approximating to three hydroxy-groups. A series of degradative experiments gave no crystallisable products.

Triacetyl-α-kosin.—α-Kosin (150 mg.) was heated on the water-bath for 2 hours with acetic anhydride (2 c.c.) and fused sodium acetate (200 mg.). The solution was poured into water and extracted with ether, and the extract washed with sodium bicarbonate solution, dried, and evaporated. The residue crystallised from light petroleum in colourless needles, m. p. 123°

[Found : C, 63·8; H, 6·5; CH_3·CO, 24·5. $C_{22}H_{25}O_4(O·CO·CH_3)_3$ requires C, 63·6; H, 6·4; CH_3·CO, 23·8%].

β-Kosin forms very pale yellow prisms, m. p. 120° [Found : C, 65·3; H, 7·0; MeO, 13·4; *M* (Rast), 356. $C_{20}H_{22}O_5(OMe)_2$ requires C, 65·4; H, 6·9; MeO, 15·3%; *M*, 404]. It is optically inactive and no crystalline degradation products could be obtained from it. Hydroxyl estimations (Zerewitinoff) gave values approximating to three hydroxy-groups at 20° and four at 95°.

Triacetyl-β-kosin.—β-Kosin (100 mg.) was acetylated in the manner described above for α-kosin. The product formed colourless needles, m. p. 155° [Found : C, 63·8; H, 6·8; CH_3·CO, 24·5. $C_{22}H_{25}O_4(O·CO·CH_3)_3$ requires C, 63·6; H, 6·4; CH_3·CO, 23·8%].

Quantitative Estimation of iso*Butyric Acid formed from Protokosin.*—(a) Protokosin (210 mg.) was refluxed for 20 minutes with 10% sodium hydroxide solution (20 c.c.), cooled, acidified with sulphuric acid, and steam-distilled. The distillate was titrated against *N*/10-sodium hydroxide (Found : C_3H_7·CO, 15·1%).

(b) Protokosin (202 mg.) was heated in a sealed tube at 160° for 6 hours with 15% sulphuric acid (6 c.c.). The product was steam-distilled, and the distillate titrated (Found : C_3H_7·CO, 15·1%).

The calculated value for one *iso*butyryl group in protokosin is C_3H_7·CO, 17·6%.

Alkali Fusion of Protokosin.—An intimate mixture of protokosin (5 g.), potassium hydroxide (10 g.), and a little water was heated for 15—20 minutes at 300°. The mixture reddened, frothed, and finally became black. The cooled melt was dissolved in water, acidified, and steam-distilled, and the residue extracted repeatedly with ether. After being decolorised with charcoal, the ethereal solution was dried and evaporated. On recrystallisation of the residue from water (charcoal), a small amount of a substance having the reactions of a phloroglucinol derivative was obtained. After several crystallisations it had m. p. 208°, undepressed by admixture with *C*-monomethylphloroglucinol (m. p. 208°); both substances had identical properties and reactions. No other crystalline product could be isolated.

We are indebted to Prof. A. Robertson for a sample of synthetic *C*-monomethylphloroglucinol.

In connection with the identification of the above product *C-monomethylphloroglucinol* was synthesised, the method described by Curd and Robertson (J., 1933, 437) being followed. We found, however, that the following modified preparation of ethyl methylphloroglucinoldicarboxylate led to considerably improved yields : To potassium ethoxide (from 1·9 g.; 2 atoms) in ether is added acetonedicarboxylic ester (5 g.), followed by ethyl methylmalonate (4·6 g.). The mixture is thoroughly shaken, and the ether cautiously evaporated. The residue is heated at 160° for 1 hour, and the solid cake cooled, dissolved in water (100 c.c.), extracted with ether, and saturated with carbon dioxide. In the course of ½ hour yellow crystals of ethyl methylphloroglucinoldicarboxylate separate. Recrystallised from alcohol, it has m. p. 90° (yield, 2 g.).

Other Experiments with Protokosin.—All known methods of methylation were applied, but only resins were obtained; similar failures were encountered on acylation, treatment with trityl chloride and phenyl *iso*cyanate. No reaction could be detected with the usual carbonyl reagents.

Oxidation experiments with chromic acid, selenium dioxide, and nitric acid gave only traces of lower fatty acids, and similar oxidation in neutral or alkaline solution with various amounts of potassium permanganate gave identical results; no oxalic acid was produced.

Catalytic hydrogenation in various solvents gave no crystalline product, although about 1 mol. H_2 seemed to be taken up; similar results were got with other reducing agents, *e.g.*, zinc; hydriodic acid and red phosphorus. Distillation with zinc dust gave only traces of a sharp-smelling oil, and no results were obtained from heating protokosin or its hydriodic acid reduction product with selenium. Numerous variations in the conditions of alkaline degradation were tried, but no products other than those above described could be isolated.

A similar lack of success attended degradation experiments of various kinds on α- and β-kosin.

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126. *Free Radicals and Atoms in Primary Photochemical Processes. The Dissociation of Aliphatic Ketones: the Acetyl Radical.*

By HAROLD H. GLAZEBROOK and THOMAS G. PEARSON.

THE photodissociation of ketones and aldehydes by light in the region 2000—3500 A. has been widely studied (Berthelot and Gaudechon, *Compt. rend.*, 1912, **155**, 204; Damon and Daniels *J. Amer. Chem. Soc.*, 1933, **55**, 2363; Norrish and Kirkbride, J., 1932, 1518; Norrish, Crone, and Saltmarsh, J., 1933, 1533; Norrish and Appleyard, J., 1934, 874), and it has been concluded (Saltmarsh and Norrish, J., 1935, 455), from the quantitative analysis of the reaction products and from the nature of the absorption spectra, that two types of decomposition are possible and usually occur simultaneously, the extent of each being governed by the symmetry of the molecule and the magnitude of the alkyl groups attached to the carbonyl. With the simpler ketones a change occurs typified by the dissociation of acetone:

$$CH_3{\cdot}CO{\cdot}CH_3 \longrightarrow C_2H_6 + CO \quad . \quad . \quad . \quad . \quad . \quad . \quad (I)$$

With higher ketones the hydrocarbon chain may break, as in the case of methyl butyl ketone, which decomposes mainly according to the equation

$$CH_3{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_3 \longrightarrow CH_3{\cdot}CO{\cdot}CH_3 + CH_2{:}CH{\cdot}CH_3 \quad . \quad . \quad . \quad (II)$$

It was also suggested (Norrish and Kirkbride, *Trans. Faraday Soc.*, 1934, **30**, 103) that in reactions of type (I) the primary act is a fission of the molecule into carbon monoxide and free alkyl radicals, a view confirmed by the characteristics of the fluorescence and absorption spectra of acetone vapour (Norrish, Crone, and Saltmarsh, J., 1934, 1456), and by the isolation of methyl, ethyl, and propyl radicals from among the primary products of the photolysis of dimethyl, diethyl, and dipropyl ketones (Pearson, J., 1934, 1718; Pearson and Purcell, J., 1935, 1151; 1936, 253; Pearson and Glazebrook, J., 1936, 1777). It is here shown that radicals also participate in the photolysis of methyl ethyl, methyl *n*-propyl, methyl *iso*propyl, di-*sec.*-butyl, and di-*tert.*-butyl ketones, and with improved technique, the smaller number of radicals in the dissociation of methyl butyl ketone has also been detected, contrary to the earlier observation (Pearson, J., 1934, 1718) that mirrors were scarcely affected, and to the conclusion that the concentration of radicals was less than one-twentieth of that of the methyl radicals resulting from acetone.

It has been found meanwhile that the activity of tellurium, arsenic, and especially lead and antimony mirrors, is diminished or completely inhibited by traces of oxygen admitted during or after their preparation. A mirror which is inactive to feeble concentrations of alkyl radicals may, however, be attacked, although slowly at first, in high concentrations such as exist in the thermal decomposition of acetone at 900°, presumably through the destruction of the oxide film by reaction with the radicals. The activity of a mirror also diminishes on standing, and to obtain reproducible results, it should be used within a few minutes of preparation. How far this is due to minute traces of oxygen given off from the walls of the apparatus, or to the crystallisation of the mirror, is not clear. The condition of the inner surface of the quartz tube exercises a considerable effect on the rate of recombination of the radicals. Tubes which have been in use for a considerable time, or have been cleaned with chromic acid mixture and insufficiently washed, or upon which there is a carbonaceous deposit, entirely prevent the passage of alkyl radicals. In the earlier experiments with methyl *n*-butyl ketone these factors were not appreciated, and only a relatively feeble source of ultra-violet light was available.

Norrish and his colleagues have estimated the contribution from reactions (I) and (II) in a number of cases from the composition of the final products of the photolyses, and we have determined directly the concentration of radicals present in these cases by comparing the times of removal of standard mirrors. The results are summarised in col. 4, Table I, Norrish's figures being added in col. 5. For purposes of comparison, we have assumed, with Norrish, that acetone dissociates wholly by way of radicals. The magnitudes of the values in cols. 4 and 5 are generally in agreement, and this is borne out by experiments in a different apparatus with di-*n*-propyl and di*iso*propyl ketones (Table II).

If reliance be placed on our relatively high value of the concentration of radicals in the dissociation of methyl ethyl and especially methyl butyl ketone, then either Norrish and his colleagues have made too low an estimate of the contribution from reaction (I), or processes other than the simple types (I) and (II) play a measurable part in the dissociation of ketones. For example, if an excited acetone molecule gives rise to ethane without the intervention of radicals, *i.e.*, $(CH_3)_2CO^* \longrightarrow C_2H_6 + CO$, this reaction would not be distinguishable from that involving dissociation into radicals by a method of assessment based on the analysis of the final reaction products. The possibility that the reaction might proceed in such a way was suggested by Damon and Daniels (*loc. cit.*), who did not, however, give free radicals any place in their reaction mechanism. Spence and Wild now include the intervention of active molecules without their dissociation into radicals as an essential part of their reaction scheme.

It is now generally recognised that the alkyl radicals participate in the reactions as a direct consequence of the primary fission of the molecule according to one of the processes $(CH_3)_2CO \longrightarrow 2CH_3\cdot + CO$, or $(CH_3)_2CO \longrightarrow CH_3\cdot CO\cdot + CH_3\cdot \longrightarrow 2CH_3\cdot + CO$.

In the absence of diacetyl from the final products of the reaction and because of the equivalence of the amounts of carbon monoxide and ethane, it was concluded that both the bonds between the carbonyl group and the two methyls are broken simultaneously (*e.g.*, Saltmarsh and Norrish, *loc. cit.*; Bamford and Norrish, J., 1935, 1505), but the intermediate formation of the acetyl radical was not excluded provided that it was short-lived and decomposed spontaneously under the experimental conditions (Norrish and Kirkbride, *Trans. Faraday Soc.*, 1934, **30**, 107; Pearson, J., 1934, 1721).

Later, Barak and Style (*Nature*, 1935, **135**, 307) found diacetyl amongst the reaction products, an observation confirmed by Spence and Wild (*ibid.*, 1936, **138**, 206), who, working at room temperature, found the volume of ethane to be always 1·5 times that of the carbon monoxide, the deficiency being accounted for by considerable quantities of diacetyl. At 60°, however, they obtained approximately equal amounts of carbon monoxide and ethane, together with some methane. They suggested that the primary process is $(CH_3)_2CO^* \longrightarrow CH_3\cdot + CH_3\cdot CO\cdot$, and that the acetyl radical is short-lived, especially at higher temperatures.

We confirmed the presence of diacetyl amongst the liquid products of the photolysis of acetone, but this is in itself only circumstantial evidence of the existence of the acetyl radical. We sought, therefore, to prepare lead acetate by allowing the products of the photolysis to impinge on lead peroxide; positive tests were obtained with the sensitive lanthanum nitrate–iodine reaction, but although the control experiments in the absence of ultra-violet light allowed the conclusion that some lead acetate had been produced, yet the results were not entirely satisfactory, for the concentrations tended towards the sensitivity limit of the test. Attempts were therefore made to establish the presence of the acetyl by indirect methods. We first confirmed Spence and Wild's observation that, although considerable amounts of diacetyl were produced when the walls of the apparatus were kept at 15°, yet no diacetyl whatever is obtained if the walls are maintained above 60°, although it is stable at this temperature. This is strong evidence that an unstable acetyl radical plays a part in the reaction, but it is just possible that different mechanisms obtain at different temperatures. We therefore removed the acetyl radical at room temperature by coating with tellurium the walls of the vessel in which the ketone was being irradiated. There were obtained only traces of diacetyl, but considerable quantities of dimethyl telluride. Control experiments showed that under the experimental conditions diacetyl passed unaffected through the apparatus.

The amounts of methyl and acetyl present during the photolysis of acetone were measured, and were comparable, so there is little doubt that below 20° the dissociation of acetone, with the formation of radicals, occurs largely according to the equation $CH_3\cdot CO\cdot CH_3 \longrightarrow CH_3\cdot + CH_3\cdot CO\cdot$. The molecular ratio $CH_3\cdot CO/Me$ is, however, greater than unity, and it was at first thought that the discrepancy could be accounted for by either of the reactions

$$CH_3 + CH_3\cdot CO\cdot CH_3 \longrightarrow C_2H_6 + CH_3\cdot CO\cdot$$
$$CH_3 + CH_3\cdot CO\cdot CH_3^* \longrightarrow C_2H_6 + CH_3\cdot CO\cdot$$

but we found that methyl radicals yield no diacetyl with acetone whether in the dark or irradiated with ultra-violet light (see also Leermakers, *J. Amer. Chem. Soc.*, 1934, **56**, 1899—absence of chains in the photolysis of gaseous acetone).

Acetyl radicals prove to have a very short life compared with alkyl radicals even at room temperature, and combine amongst themselves or with methyl, react with acetone, or dissociate on each collision (or after very few collisions) with the walls of the quartz tube, so that they are unable to traverse appreciable distances from the irradiated zone.

Experimental.

Materials.—Acetone from the sodium iodide compound was dried with calcium chloride and fractionally distilled in a vacuum; b. p. 56·1°.

The other ketones were dried with calcium chloride and fractionally distilled through a bead column at atmospheric pressure, the fractions boiling between proper limits being collected: methyl ethyl ketone, b. p. 79·5°; methyl *n*-propyl ketone, b. p. 101·5—102°; methyl *iso*propyl ketone, b. p. 92—94°; methyl *n*-butyl ketone, kindly provided by Dr. G. A. R. Kon, b. p. 126—127·5°; di-*sec.*-butyl ketone, b. p. 163—164·5°. Di-*tert.*-butyl ketone, b. p. 148—150°, was prepared by the successive methylation of pinacolone (Haller and Bauer, *Compt. rend.* 1910, **150**, 582). It was found that the yield was increased from 17% to 40% by carrying out the reaction entirely in benzene instead of using ether for the first two stages. These purified specimens were redistilled in a vacuum immediately before use, with the rejection of about a quarter of each in head and tail fractions.

Alkyl Radicals from Aliphatic Ketones.—The apparatus used for detecting and measuring the concentrations of the radicals was similar to a previous one (J., 1935, 1153), but butyl phthalate manometers were employed. A single hot mercury-vapour arc (100 v., 4·5 amps.) served as a source of ultra-violet light. In a quartz tube of 12 mm. diameter, with the vapours entering the tube at 1—4 mm. pressure, and at velocities of 15—20 m./sec., opaque tellurium mirrors 2 mm. wide situated 4 cm. from the irradiated zone were removed in less than 4 mins. by the radicals from all the ketones mentioned above.

Repeated efforts were made to identify the radicals from di-*tert.*-butyl ketone. Unfortunately, the properties of the metal *tert.*-butyls are imperfectly known, nor do they lend themselves readily to identification, and although with mercury traces of an evil-smelling compound were obtained which combined with mercuric bromide to yield a substance which melted with decomposition in the range 105—110° (di-*tert.*-butylmercury bromide, m. p. 106°, decomp.), we do not regard the result as more than an indication. There was, however, no evidence of mercury-methyl, -ethyl, or -propyl, which should have been easily detected had they been present.

The concentrations of radicals occurring during the photolysis of a number of ketones were compared by observing the times of disappearance of standard tellurium mirrors situated at a constant distance along the quartz tube from the light source, the ketones being admitted to the tube at the same pressure. The results are recorded in Tables I and II.

Table I.

Pressure at beginning of tube, 0·7 mm. Hg. Diameter of tube, 12 mm.

Ketone.	No. of expts.	Time of removal, t secs.	Relative concn. = $6500/t$.	Extent of type (I) reaction (Norrish *et al.*).
Dimethyl	5	65	100	100
Methyl ethyl	5	80	81	70—80
Methyl *n*-propyl	8	105	62	—
Methyl *n*-butyl	8	225	28	10

Table II.

[Calculated from data previously recorded (J., 1936, 1779).]

Pressure at beginning of tube, 0·9 mm. Hg. Diameter of tube, 11·2 mm.

Ketone.	Time of removal, t secs.	Relative concn. = $3700/t$.	Extent of type (I) reaction (Norrish *et al.*).
Di-*n*-propyl	100	37	37
Di*iso*propyl	90	41	44

The Acetyl Radical.—The apparatus used was a modification of that previously described (J., 1936, 254, Fig. 2). Instead of the narrow joint A, a piece of quartz tubing equal in diameter to that at D was sealed on. This was fitted with a ground joint connected directly to a liquid-

air trap, and the whole was incorporated in an apparatus similar to that shown in Fig. 1, J., 1935, 1153, in place of the quartz tube *XZ*, so that the acetone vapour could pass in either direction through the quartz irradiation vessel. A single hot mercury-vapour arc was situated in *C* (Fig. 2, J., 1936, 254), and butyl phthalate manometers were used to avoid the presence of mercury in the apparatus. After the system had been thoroughly dried, acetone was introduced into the small fractionating vessel *J* containing phosphoric anhydride, out-gassed by cooling in liquid air and pumping, and kept for at least 12 hours at $-80°$. A small head fraction was removed before distilling the main volume of the liquid into a second vessel, and a few c.c. of tail fraction were left behind.

The acetone was streamed at a pressure of a few mm. of mercury through the quartz vessel of which the outer surface was covered with tin-foil, and irradiated. After passing backwards and forwards six times, the acetone had acquired a strong greenish-yellow colour and smelt of diacetyl. In a second experiment, after 52 passages with 30 c.c. of acetone, the liquid was fractionated from a vessel at $-90°$ to one in liquid air. The distillate was colourless until only about 1 c.c. remained. This residue was shaken with an excess of dinitrophenylhydrazine; a yellow precipitate was obtained, consisting largely of the acetone derivative, which was removed by extraction with boiling alcohol. An orange residue was left, too small to be recrystallised, which had m. p. 310—314° (m. p. of diacetyl derivative, 312°). During these experiments the cooling water was kept below 15°. They were repeated, but by using a slower rate of circulation of the water in the jacket, the walls were held at about 60°. No diacetyl could be detected after 10 passages of the acetone through the irradiated zone.

We tried to identify the acetyl radicals by allowing them to react with lead peroxide. In the first experiment, the lead peroxide was situated at *A* and *D*, and in later experiments, in view of the short life of the radical (see p. 571), the whole of the inner surface of the outer wall was covered with it. After 15 passages of acetone with the mercury arc running, the apparatus was dismantled, and the lead peroxide extracted first with 3 c.c. of distilled water, then separately with 5 c.c. of very dilute hydrochloric acid. The extracts were tested for acetate with lanthanum nitrate and iodine (Feigl, " Qualitative Analyse mit Hilfe von Tüpfelreaktionen," 1935, p. 408), and a positive reaction was obtained, but it was close to the sensitivity limit of the test (50γ per drop), and scarcely distinguishable from the results of the blank experiments.

In order to remove the acetyl radical at the room temperature, the inner surface of the outer wall of the irradiation vessel was completely covered with sublimed tellurium. This was done by cooling the outer wall of *B* with water while a Bunsen flame played up the centre *C*, and subliming tellurium from the bottom of *B* by means of a blowpipe flame. After 12 passages, so much of the mirror had been eaten away that it became patchy, and the experiment had to be discontinued. The product was a yellow liquid, smelling strongly of dimethyl telluride, which was removed by adding a solution of mercuric chloride in acetone, and filtering off the white flocculent precipitate of dimethyl telluride mercurichloride. The filtrate had a barely perceptible green colour. In another experiment, mercury iodide was used instead of chloride, and a canary-yellow precipitate was deposited identical in appearance with dimethyl telluride mercuri-iodide, again leaving only a very faintly green solution.

Evidently, the tellurium had effected practically quantitative removal of the diacetyl, probably through the simple dissociation $CH_3{\cdot}CO \longrightarrow CH_3{\cdot} + CO$, although an acetyl telluride may have been formed which we were unable to detect.

Since, after the removal of dimethyl telluride there is no other coloured product but diacetyl, it may be estimated colorimetrically. Two parallel series of experiments were therefore made in which the inner surface of the outer wall of the irradiation vessel was (*a*) left blank and (*b*) entirely covered with tellurium. In each complete experiment, ten passages of ketone were made under identical conditions, and the liquid products at room temperature were treated with 5 c.c. of a saturated solution of mercuric iodide in dry acetone.

After standing for at least 3 hours to ensure complete precipitation, the liquids were filtered through a weighed Pregl micro-filter. Any mercuri-iodide precipitate on the filter was washed three times with pure cold acetone, dried in a vacuum (Hyvac) at the room temperature for 5 minutes, and weighed. The clear filtrate was distilled from the excess of mercuric iodide, and the quantity of diacetyl in the distillate determined colorimetrically by comparison with a freshly prepared solution of diacetyl in acetone (2 mg. per c.c.). The results are shown below :

	$(CH_3{\cdot}CO)_2$, mg.	$CH_3{\cdot}CO$, mols. $\times 10^4$.	$TeMe_2,HgI_2$, mg.	CH_3, mols. $\times 10^4$.
Surface blank	4·8	1·11	none	none
Surface covered with Te	0·86	0·20	25·28	0·85

Before interpreting these data, it was necessary to establish that tellurium in the presence of ultra-violet light has no influence on diacetyl already formed, so the experiment was modified by having only the lower half of the surface of the irradiation vessel covered with the element. The product from ten runs was greenish-yellow and, after precipitation of the dimethyl telluride, was found to contain about half the amount of diacetyl yielded with the blank surface. It was noted that mercuric halides are without apparent action on solutions of diacetyl in acetone.

The results recorded above can only be given a roughly quantitative interpretation. If it is assumed that every acetyl radical formed yields diacetyl, and that every methyl or acetyl radical impinging on tellurium reacts to form dimethyl telluride, then it is clear that the molar quantity of acetyl produced is comparable with that of methyl.

The difficulty of reproducing experimental conditions in a large apparatus which must be dismantled, cleaned, and reassembled for each series of experiments cannot be overlooked.

To ascertain whether the large yield of acetyl was due to the reaction $CH_3\cdot + CH_3\cdot CO\cdot CH_3 \longrightarrow CH_3\cdot CO\cdot + C_2H_6$, the acetone was passed through a furnace at *A*, then rapidly cooled by running water over the outside of the tube, before entering the irradiated zone. Although there was a high concentration of methyl radicals in the gases leaving the furnace, the yield of diacetyl was not perceptibly increased above that obtained without the furnace. No diacetyl was obtained with the furnace, but without subsequent irradiation of the acetone, so that the reaction being sought is equally unlikely.

We tried to estimate the life-period of the acetyl radical by forming mirrors in the side arms of the apparatus at *A* and *D* (J., 1936, 254) just where the streaming gas leaves the irradiated zone. Although considerable amounts of dimethyl telluride were formed (12 runs, 7·26 mg. of dimethyl telluride mercuri-iodide), there was no perceptible diminution in the yield of diacetyl, so even under our conditions of high streaming velocity (19·2 m./sec. at beginning of tube) no acetyl leaves the irradiated zone, and recombination or decomposition must occur quantitatively in, or on the walls of, the irradiation vessel; hence, compared with the alkyl radicals, acetyl has a very short life (less than 10^{-4} sec.) in the presence of a silica surface, although on the average, acetyl radicals evidently survive more than 100 collisions with other molecules in the gas phase before combining on the walls to yield diacetyl.

An endeavour to refine the experiment by irradiating the acetone as it streamed through a straight quartz tube was unsuccessful because even after 28 runs (in the absence of tellurium) the greenish-yellow colour due to diacetyl was too faint for colorimetric comparisons, and extension of the number of experiments beyond 28 to fix each point made the method impracticably tedious.

SUMMARY.

The relative quantities of radicals present during the photolysis of acetone, methyl ethyl, methyl *n*-propyl, methyl *iso*propyl, methyl *n*-butyl, di-*n*-propyl, and di*iso*propyl ketones have been measured, and radicals have been obtained from di-*tert*.-butyl and di-*sec*.-butyl ketones.

The acetyl and methyl radicals are formed in comparable quantities during the photodissociation of acetone by ultra-violet light at room temperature. Acetyl radicals rapidly combine with one another to form diacetyl. Under our experimental conditions acetyl has a short life compared with the alkyl radicals; it is quantitatively decomposed on a silica surface at 60°, and is removed by tellurium at the room temperature.

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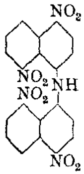
127. *Synthesis of 8 : 8'-Dinitro-1 : 1'-dinaphthyl and Related Compounds.*

By HERBERT H. HODGSON and J. HAROLD CROOK.

FROM a study of the reactivities of various iodonitronaphthalenes with copper-bronze, Cumming and Howie (J., 1931, 3176) concluded that dinaphthyl formation only occurred when both the nitro-group and the iodine atom were in the same nucleus. Salkind also (*Ber.*, 1931, **64**, 289) claimed that the influence of a nitro-group in producing high reactivity in a halogen atom did not extend from one ring to the other of the naphthalene nucleus. The present investigation, however, has established that 8 : 8'-*dinitro*-1 : 1'-*dinaphthyl*

is formed in a 43·5% yield when 1-*iodo-8-nitronaphthalene* is boiled with copper-bronze in nitrobenzene solution, a result which indicates considerable activation of the iodine in the 1-position by the *peri* (8)-nitro-group with respect to anionoid reagents. The intensity of activation, however, is less than in the case of 1-iodo-2-nitronaphthalene, which, under similar (though not identical) conditions affords a 70% yield of the corresponding dinaphthyl (Cumming and Howie, *loc. cit.*).

Two general methods are now described for the preparation of 8 : 8′-dinitro-1 : 1′-dinaphthyl and related substances : (1) The treatment of 8-nitro-1-naphthalenediazonium sulphate or derivatives with a neutral suspension of cuprous hydroxide, and (2) the action of copper-bronze on 1-iodo-8-nitronaphthalene or its derivatives. By these means 4 : 4′-*dibromo*-8 : 8′-*dinitro*-1 : 1′-*dinaphthyl* was readily formed from 4-bromo-1-iodo-8-nitronaphthalene, but in attempts to prepare 4 : 8 : 4′ : 8′-*tetranitro*-1 : 1′-*dinaphthyl* by the decomposition of 4 : 8-dinitro-1-naphthalenediazonium sulphate with cuprous hydroxide the reaction took an entirely different course and 4 : 8 : 4′ : 8′-*tetranitro*-1 : 1′-*dinaphthylamine* (I) resulted. Such a decomposition of diazonium salts appears to be new and could hardly have been anticipated. This tetranitrated diphenylamine appears to be a *ψ*-acid, since, like 2 : 2′ : 4 : 4′ : 6 : 6′-hexanitrodiphenylamine (aurantia), it readily dissolves in aqueous alkaline hydroxides to give highly coloured solutions, indicating salt formation.



(I.)

4 : 8 : 4′ : 8′-Tetranitro-1 : 1′-dinaphthyl was readily formed from 1-*iodo*-4 : 8-*dinitronaphthalene* by the copper-bronze procedure.

The melting point of 1-iodo-8-nitronaphthalene (80°) is much lower than that of the chloro- (94°) and the bromo- (99—100°) analogue, and may indicate chelation between the iodine atom and the nitro-group. Such chelation could readily occur, since the *peri*-positions are nearer together than the ortho-positions (Mills and Elliott, J., 1928, 1291).

8-Nitro-1-naphthylamine was found to be readily diazotisable either in glacial acetic acid solution by means of nitrosylsulphuric acid (Hodgson and Walker, J., 1933, 1620) or by the ordinary procedure in dilute sulphuric acid, thereby differing from the 2- and 4-isomerides, which require the former method. This fact, taken in conjunction with the reduced activity of the iodine in the *peri*-position in 1-iodo-8-nitronaphthalene compared with that in the 2-nitro-isomeride, would suggest a direct effect (— *D*) of the nitro-group through space, rather than a relayed inductive effect (— *I*) *via* the carbon atoms of the nucleus.

Experimental.

1-*Iodo*-8-*nitronaphthalene*.—8-Nitro-1-naphthylamine (9·4 g., 0·05 mol.), dissolved in glacial acetic acid (100 c.c.), was added to a solution of sodium nitrite (3·8 g.) in concentrated sulphuric acid (40 c.c.) at 10—15°. The mixture was vigorously stirred for 10 minutes and then added to an ice-cold solution of potassium iodide (10 g.) in water (40 c.c.). The light brown 1-*iodo*-8-*nitronaphthalene* thereby precipitated was recrystallised from ligroin (b. p. 80—100°) and then from alcohol or glacial acetic acid, and obtained in large, pale yellow needles, m. p. 80° (Found : I, 42·2. $C_{10}H_6O_2NI$ requires I, 42·5%). The brown impurity in the crude product could not be removed except by crystallisation from ligroin.

1-*Iodo*-4 : 8-*dinitronaphthalene*.—(a) Finely powdered 1-iodo-8-nitronaphthalene (3 g.) was added gradually to a mixture of nitric acid (15 c.c., *d* 1·4) and fuming nitric acid (5 c.c., *d* 1·5) at 0—10°. After 2 hours' stirring at 15°, the 1-*iodo*-4 : 8-*dinitronaphthalene* (3·2 g.) was precipitated by the addition of water; it crystallised from glacial acetic acid in pale yellow needles, m. p. 146° (Found : I, 36·8. $C_{10}H_5O_4N_2I$ requires I, 36·9%). Iodine was evolved when the nitration was attempted with nitric acid (*d* 1·5) alone.

(b) 4 : 8-Dinitro-1-naphthylamine (2 g.) was precipitated from its solution in boiling glacial acetic acid (20 c.c.) by rapid cooling, and the resulting suspension diazotised by adding it to a solution of sodium nitrite (1·0 g.) in concentrated sulphuric acid (10 c.c.). After 10 minutes' stirring, the diazo-solution was poured into one of potassium iodide (2·0 g.) in water (20 c.c.) initially at 15°. The resulting light brown precipitate was recrystallised first from ligroin and then from glacial acetic acid; m. p. and mixed m. p. with product from (a) 146° (Found : I, 36·6%).

8 : 8'-*Dinitro*-1 : 1'-*dinaphthyl*.—(a) 8-Nitro-1-naphthylamine (18 g.) was boiled with concentrated sulphuric acid (30 c.c.) and water (80 c.c.) until dissolution occurred; the fine suspension of the sulphate which resulted on rapid cooling to 0° was diazotised by the addition, below the surface, of a solution of sodium nitrite (7·0 g.) in water (14 c.c.). An aqueous suspension of cuprous hydroxide was prepared by the addition of 20% aqueous sodium hydroxide to a solution of cuprous chloride (30·0 g.) in concentrated hydrochloric acid (120 c.c.) until the mixture was faintly alkaline, the precipitate being washed by decantation until no alkaline reaction was given. The above diazo-solution was then added at 15—20° with stirring, the mixture heated on the water-bath for 15 minutes, and the solid collected and repeatedly extracted with dilute aqueous ammonia to remove copper compounds. The dried material was boiled under reflux with just sufficient nitrobenzene to effect solution; 8 : 8'-*dinitro*-1 : 1'-*dinaphthyl* separated from the filtered solution in well-defined brown prisms (5·4 g.; 32·8% yield), which were recrystallised from the same solvent and, after being washed with methyl alcohol, obtained in pale lemon-yellow prisms, m. p. 295° (Found : N, 8·1. $C_{20}H_{12}O_4N_2$ requires N, 8·1%). The product was liable to contain an azo-compound, since an intense violet-red coloration was obtained on warming with concentrated sulphuric acid. This impurity, however, could be removed by recrystallisation from nitrobenzene until the product afforded only a dull green colour with concentrated sulphuric acid.

(b) Copper-bronze (1·5 g.) and 1-iodo-8-nitronaphthalene (4 g.) were refluxed in nitrobenzene (20 c.c.) for 1¼ hours; the hot filtered solution deposited almost pure 8 : 8'-dinitro-1 : 1'-dinaphthyl (1 g.; 43·5% yield) on cooling, m. p. and mixed m. p. with the product from (a) 295° (Found : N, 8·2%). The dinaphthyl was insoluble in boiling methyl or ethyl alcohol, very slightly soluble in boiling glacial acetic acid (*ca.* 1 g. in 300 c.c.), but more soluble in boiling tetrahydronaphthalene, aniline, nitrobenzene and cellusolve (*ca.* 1 g. in 100 c.c.).

4 : 8 : 4' : 8' :-*Tetranitro*-1 : 1'-*dinaphthyl*.—1-Iodo-4 : 8-dinitronaphthalene (4 g.) was refluxed for 30 minutes with copper-bronze (2 g.) in nitrobenzene (30 c.c.). The cooled filtered solution deposited light brown crystals (0·9 g.; 36% yield) of 4 : 8 : 4' : 8'-*tetranitro*-1 : 1'-*dinaphthyl*, which separated from nitrobenzene in very pale yellow prisms, m. p. 260° (bath initially at 250°). The pale yellow liquid obtained at 260° became dark on further heating, resolidified, and melted again at 270—280° (Found : N, 13·2. $C_{20}H_{10}O_8N_4$ requires N, 12·9%). Slow heating gave m. p. 260° with darkening and evolution of gas. Warm concentrated sulphuric acid was coloured port-wine red by this substance.

4 : 4'-*Dibromo*-8 : 8'-*dinitro*-1 : 1'-*dinaphthyl*.—(a) 4-Bromo-8-nitro-1-naphthylamine (5 g.) was dissolved in boiling glacial acetic acid (50 c.c.), mixed ice-cold with concentrated sulphuric acid (30 c.c.) and water (100 c.c.), sodium nitrite (3 g.), dissolved in water (10 c.c.), added with stirring at 0—5°, and the diazo-solution mixed with a neutral suspension of cuprous hydroxide prepared as described above from cuprous chloride (7·5 g.). The resulting 4 : 4'-*dibromo*-8 : 8'-*dinitro*-1 : 1'-*dinaphthyl* crystallised from nitrobenzene in yellow prisms, m. p. 294° (decomp.) (Found : Br, 32·0. $C_{20}H_{10}O_4N_2Br_2$ requires Br, 31·9%).

(b) 4-Bromo-1-iodo-8-nitronaphthalene (2·5 g.) and copper-bronze (1·0 g.) were refluxed in nitrobenzene for 1 hour; 4 : 4'-dibromo-8 : 8'-dinitro-1 : 1'-dinaphthyl (0·5 g.; 29% yield) crystallised from the cooled filtered solution and formed pale yellow prisms, m. p. and mixed m. p. with product from (a) 294° (decomp.), on recrystallisation from nitrobenzene (Found : Br, 31·8%).

Attempted Preparation of 2 : 4 : 2' : 4'-*Tetrabromo*-8 : 8'-*dinitro*-1 : 1'-*dinaphthyl*.—2 : 4-Dibromo-1-iodo-8-nitronaphthalene (5 g.) was refluxed with copper-bronze (20 g.) in nitrobenzene (20 c.c.) for 30 minutes. The solution obtained was unworkable owing to the large amount of colloidal matter present.

4 : 8 : 4' : 8'-*Tetranitro*-1 : 1'-*dinaphthylamine*.—4 : 8-Dinitro-1-naphthylamine (4·6 g.) was diazotised as above, and the diazo-solution treated with an aqueous suspension of cuprous hydroxide prepared from cuprous chloride (7·5 g.). The *product* (1·3 g.; 29% yield) crystallised from nitrobenzene in colourless plates, m. p. 244° (Found : N, 15·5. $C_{20}H_{11}O_8N_5$ requires N, 15·6%), which were readily soluble in aqueous sodium hydroxide to give a yellow colour in dilute and a red colour in more concentrated solutions, and precipitated therefrom unchanged by dilute hydrochloric acid; no acetyl derivative could be obtained.

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TECHNICAL COLLEGE, HUDDERSFIELD. [*Received, February 27th*, 1937.]

128. *The Conductivity of Univalent Electrolytes in Water.*

By Robert A. Robinson and Cecil W. Davies.

Some years ago an empirical equation was put forward (Davies, *Trans. Faraday Soc.*, **1927**, **23**, 351) which represented with fair accuracy, up to a concentration of at least $1 \cdot 0N$, the conductivity figures of Kohlrausch for a number of completely dissociated uni-univalent salts at 18°. The value of this equation lay in the fact that it was free from any arbitrary constant dependent on the nature of the salt, so that it could be utilised as a standard of behaviour to which all normal completely dissociated salts could be expected to conform. The basis of this equation has not been regarded with much confidence by some later writers on the subject, and it therefore seemed of interest to apply to it a further test rendered possible by the accurate measurements of Shedlovsky (*J. Amer. Chem. Soc.*, **1932**, **54**, 1411) on lithium, sodium, potassium, and hydrogen chlorides at 25°.

Before discussing the data at higher concentrations, it will be necessary to consider those for the most dilute solutions. In a previous paper (Davies, this vol., p. 432) it has been shown that the equation proposed by Shedlovsky for potassium chloride does not agree as closely as it should with the measurements for the most dilute solutions, and leads to a Λ_0 value that is too low by 0·04%. The same is true for sodium chloride. The ten measurements made by Shedlovsky * below $0 \cdot 001N$ agree somewhat better with the equation $\Lambda = 126 \cdot 50 - 88 \cdot 56\sqrt{C} + 40C$, than with the Shedlovsky equation, which gives $\Lambda_0 = 126 \cdot 46$. The results for dilute hydrochloric acid solutions are more erratic, but appear to lead to $\Lambda_0 = 426 \cdot 25$ or 426·3 rather than to the value 426·16 derived by Shedlovsky, and in the same way the value $\Lambda_0 = 115 \cdot 11$ for lithium chloride is preferred to Shedlovsky's value 115·03. These values are used in the following calculations.

The empirical equation previously proposed was based on the discovery that at concentrations too high for Onsager's limiting equation $\Lambda_0 - \Lambda = b\sqrt{C}$ to be obeyed, the conductivity decrease was still proportional to the factor b, the Onsager slope. The dependence of the conductivity on concentration was complex, and the relation was used in the form $\Lambda_0 - \Lambda = b \,.\, f(C)$, where the value of $f(C)$ at any concentration had to be

Table I.

C	0·001	0·002	0·005	0·01	0·02	0·05	0·07	0·10
$f(C)$	0·03122	0·04382	0·06683	0·09112	0·12254	0·17531	0·19708	0·22350
$(\sqrt{C} - C + 0 \cdot 001)$	0·03162	0·04372	0·06671	0·09100	0·12242	0·17461	0·19558	0·21723
Lithium chloride : $\Lambda_0 = 115 \cdot 11$; $b = 85 \cdot 95$.								
Λ, obs.	112·46	111·35	109·36	107·31	104·55	100·12	98·14	95·86
Λ, calc.	112·43	111·34	109·36	107·28	104·58	100·04	98·17	95·89
Δ	+0·03	+0·01	±0	+0·03	−0·03	+0·08	−0·03	−0·03
Sodium chloride : $\Lambda_0 = 126 \cdot 50$; $b = 88 \cdot 53$.								
Λ, obs.	123·76	122·71	120·62	118·47	115·69	110·92	—	106·72
Λ, calc.	123·74	122·62	120·58	118·43	115·66	110·99	—	106·72
Δ	+0·02	+0·09	+0·04	+0·04	+0·03	−0·07	—	±0
Potassium chloride : $\Lambda_0 = 149 \cdot 92$; $b = 93 \cdot 85$.								
Λ, obs.	146·97	145·83	143·68	141·36	138·38	133·37	—	128·94
Λ, calc.	146·99	145·81	143·65	141·37	138·42	133·47	—	128·94
Δ	−0·02	+0·02	+0·03	−0·01	−0·04	−0·10	—	±0
Hydrochloric acid : $\Lambda_0 = 426 \cdot 27$; $b = 156 \cdot 7$.								
Λ, obs.	421·36	419·39	415·80	412·00	407·23	399·08	395·44	391·31
Λ, calc.	421·38	419·40	415·79	411·99	407·07	398·80	395·38	391·24
Δ	−0·02	−0·01	+0·01	+0·01	+0·16	+0·28	+0·06	+0·07

evaluated from the data for one or more salts. The equation is now applied to Shedlovsky's figures in Table I; this shows the values of $f(C)$ which best fit the data, and the subsequent

* All Shedlovsky's values quoted in this paper have been increased by 0·028% in order to convert them to the new Jones and Bradshaw standard (cf. Shedlovsky and Brown, *J. Amer. Chem. Soc.*, **1934**, **56**, 1069).

rows of figures show, for each of the chlorides investigated by Shedlovsky, the degree of agreement between the conductivity calculated from the Λ_0, b, and $f(C)$ values shown, and the observed conductivity, taken from a curve of the experimental results in the case of lithium chloride, and from Table 6 of Shedlovsky's paper for the other three electrolytes. The agreement is very satisfactory; it is as good, in fact, as the agreement between the observed values and the values calculated from Shedlovsky's equations, although these contain an additional arbitrary constant that varies from salt to salt. The empirical equation can therefore be applied with some confidence to any univalent electrolyte at 25°, using the $f(C)$ values listed in Table I. For intermediate values of the concentration, $f(C)$ can be found by interpolation; but between 0·002N and 0·02N, $f(C)$ is satisfactorily represented by $f(C) = \sqrt{C} - (C - 0{\cdot}001)$, as is shown in the table.

Shedlovsky has also examined potassium nitrate, a salt which does not show a normal conductivity curve, and for which a dissociation constant $K = 1{\cdot}3$ has been derived from the conductivities at 18°. For this salt the figures at the lower concentrations, when plotted by the method of Onsager (*Physikal. Z.*, 1927, **28**, 277), give $\Lambda_0 = 144{\cdot}90$. The conductivities at the higher concentrations are uniformly lower than the values calculated by the empirical equation just discussed, and if the discrepancy is attributed to incomplete dissociation, and the dissociation constant calculated in the usual way (Davies, "Conductivity of Solutions," 1933, p. 109), the results shown below are obtained :

Potassium nitrate : $\Lambda_0 = 144{\cdot}90$.

C	0·01	0·02	0·05	0·07	0·10
Λ	135·82	132·41	126·31	123·56	120·40
Λ_x	136·46	133·56	128·79	126·78	124·38
α	0·9954	0·9914	0·9808	0·9746	0·9680
K	1·72	1·68	1·60	1·59	1·66

Here, C represents the equivalent concentration and Λ the observed conductivity; Λ_x, found by successive approximations, is the conductivity that a solution of this ionic concentration should have according to our equation, α is the degree of dissociation, and K, the dissociation constant, is $f^2\alpha^2C/(1 - \alpha)$, where f, the ion-activity coefficient, has been taken from the data of Robinson (*J. Amer. Chem. Soc.*, 1935, **57**, 1165). The values of K are satisfactorily constant.

The results of applying the same treatment to silver nitrate are as follows :

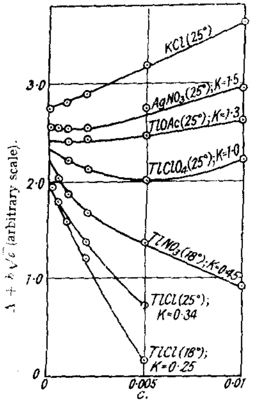
Silver nitrate : $\Lambda_0 = 133{\cdot}42$.

C	0·01	0·02	0·05	0·10
Λ	124·76	121·41	115·24	109·14
Λ_x	125·22	122·41	117·80	113·56
α	0·9963	0·9918	0·9783	0·9611
K	2·14	1·76	1·48	1·45

The last two values, corresponding to solutions in which more than 1% of the salt is undissociated, are much more reliable than the first two, but the variations of K are not covered in this case by the probable error of the conductivity measurements, and it is possible that the treatment of this salt is complicated by the presence of complex ions, since the transference numbers reported by McInnes, Shedlovsky, and Longsworth (*Chem. Rev.*, 1933, **13**, 29) are also abnormal. The value found from the data at 18° was $K = 1{\cdot}20$, there being no evidence of a change of K with changing concentration.

Conductivity Measurements with Thallous Salts.—Other interesting cases in which anomalous conductivities find a reasonable explanation in incomplete dissociation occur with thallous salts. Davies has already shown that this is true of the chloride and nitrate at 18°, and Robinson (*J. Amer. Chem. Soc.*, 1937, **59**, 84) has suggested that the very low activity and osmotic coefficients of thallous perchlorate and acetate at 25° may also be due to incomplete dissociation. We have now measured the conductivities of thallous perchlorate and acetate at 25° up to a concentration of 0·01N. The salts were prepared from the purified carbonate, and recrystallised three times, conductivity water being used for the last recrystallisation. The apparatus and methods employed in the conductivity measure-

ments have been described in a previous paper (Davies, this vol., p. 432). Two runs were made with each salt, and the experimental figures are given in Table II. For thallous perchlorate the normal solvent correction has been applied, but for thallous acetate a combined solvent and hydrolysis correction was necessary, and this has been calculated by a method previously outlined (Davies, *Trans. Faraday Soc.*, 1932, **28**, 607), it being assumed that a small part (0·07 gemmho) of the solvent's conductivity was attributable to saline impurities and that the residue (0·47 gemmho for Run 3, and 0·37 gemmho for Run 4) was due to carbon dioxide.



($\Lambda + b\sqrt{c}$) calculated from Onsager's equation for various electrolytes.

TABLE II.

Conductivities of Thallous Perchlorate and Acetate at 25°.

Thallous perchlorate (M = 303·85).

Run No.	$C \times 10^4$.	Λ.	Run No.	$C \times 10^4$.	Λ.
1	1·7372	141·36	1	37·436	136·71
2	4·0891	141·16	2	58·103	135·45
1	9·823	139·71	1	77·535	134·32
1	18·999	138·45	2	98·002	133·42
2	26·049	137·76			

Thallous acetate (M = 263·41).

Run No.	$C \times 10^4$.	Λ.	Run No.	$C \times 10^4$.	Λ.
4	4·3160	113·84	4	48·560	109·73
3	6·4852	113·42	3	58·726	109·10
4	11·584	112·78	4	78·072	108·16
3	21·956	111·62	3	93·088	107·61
4	28·086	110·10	4	147·34	105·24
3	40·553	110·21			

From a graph of these results we have read off conductivities at round concentrations and thence calculated ($\Lambda + b\sqrt{c}$) from Onsager's equation. These values of ($\Lambda + b\sqrt{c}$) are plotted against the concentration in the figure, which also shows similar plots for a typical, completely dissociated salt, potassium chloride, and an incompletely dissociated electrolyte, silver nitrate. For comparison, data for thallous chloride and nitrate are also included, the values of Kohlrausch and Steinwehr (*Sitz. Berl. Akad.*, 1902, 581) and of Bray and Winninghof (*J. Amer. Chem. Soc.*, 1911, **33**, 1663) being used. This method of plotting conductivity results not only makes it possible to decide whether a salt is completely dissociated or not, but also gives an approximate estimate of the degree of dissociation and the dissociation constant.

TABLE III.

	Thallous chloride at 18°.			Thallous chloride at 25°.			
C	0·002	0·005	0·01	0·002	0·005	0·01	0·01607
α	0·9928	0·9830	0·9698	0·9952	0·9886	0·9757	0·9642
K	0·25	0·24	0·25	0·37	0·36	0·31	0·31

	Thallous nitrate at 18°.			Thallous perchlorate at 25°.			Thallous acetate at 25°.		
C	0·002	0·005	0·01	0·002	0·005	0·01	0·002	0·005	0·01
α	0·9955	0·9912	0·9843	0·9982	0·9958	0·9931	0·9985	0·9978	0·9941
K	0·39	0·47	0·48	1·00	1·00	1·14	1·20	1·32	1·33

The conductivity values at infinite dilution are 115·63 for thallous acetate and 142·65 for the perchlorate. Taking Λ_0(KCl) = 149·92, Λ_0(Cl) = 76·39, and Λ_0(NaCl) = 126·50,

we have Λ_0(Na) = 50·11, and if from MacInnes and Shedlovsky's results (*J. Amer. Chem. Soc.*, 1932, **54**, 1429) we use Λ_0(NaOAc) = 91·03, then Λ_0(OAc) = 40·92, Λ_0(Tl) = 74·71, and $\Lambda_0(ClO_4)$ = 67·94.

Table III gives the degree of dissociation and dissociation constant for some thallous salts, calculated in the same way as for potassium and silver nitrates.

SUMMARY.

It is shown that the change of conductivity with concentration in the case of lithium, sodium, potassium, and hydrogen chlorides at 25° can be expressed within the experimental error by: (1) Onsager's limiting equation up to 0·001N, (2) the equation $\Lambda = \Lambda_0 - b(\sqrt{C} - C + 0{\cdot}001)$ between 0·002 and 0·02N, and (3) the equation $\Lambda = \Lambda_0 - b \, . \, f(C)$ above 0·02N, $f(C)$ being an empirical function of the concentration and the same for all electrolytes.

The data for potassium and silver nitrates are anomalous but can be accounted for by assuming incomplete dissociation, K being 1·6 and 1·5 respectively at 25° compared with 1·3 and 1·2 at 18°.

The conductivities of solutions of thallous perchlorate and acetate have been measured at 25° up to a concentration of 0·01N, and the dissociation constants of a number of thallous salts have been calculated.

BATTERSEA POLYTECHNIC, LONDON, S.W. 11. [*Received, March 8th, 1937.*]

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129. *Polysaccharides. Part XXIII. Determination of the Chain Length of Glycogen.*

By W. N. HAWORTH, E. L. HIRST, and F. A. ISHERWOOD.

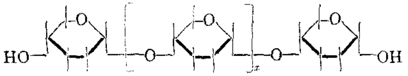
IN Part XI (Haworth and Percival, J., 1932, 2277) a study of the molecular structure of glycogen provided evidence of the structural relationship of this polysaccharide to starch. Whereas for starch the chemical assay of the end group has revealed in every case hitherto examined a chain of 24—30 glucose units, we had found for glycogen a value corresponding to 12 glucose units. Recently, in examining specimens of glycogen from a variety of sources, we encountered (from rabbit liver) glycogen which gave values for the chain length differing from those we had previously observed for this polysaccharide. The results now described are concerned with these specimens, which are exceptional in that they reveal by the end-group method the presence of approximately 18 glucose units in the chain. A preliminary account of these observations was given by one of the authors (Haworth, Pres. Add. Chem. Sec. Brit. Association, 1935, p. 41) where it was pointed out that glycogen had been shown to possess, in different specimens, a chain length of 12 or 18 glucose units. The experimental data which form the basis of these results are now appended. It will be seen that control experiments were instituted in the endeavour to expose any source of error in the chain length determination. It is now clear that there exist at least two types of glycogen which display no essential differences in structure or general properties excepting only the chain length as determined by the method of end-group assay. Since the above conclusions were recorded by one of us a similar specimen of glycogen containing also 18 glucose units has been described by Bell (*Biochem. J.*, 1936, **30**, 1612).

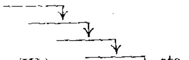
On the subject of the particle size of glycogen and starch, experiments have been conducted in this laboratory by Carter and Record (*J. Soc. Chem. Ind.*, 1936, **55**, 218) which suggest that glycogen and starch may exist in a very highly aggregated form, amounting in the case of glycogen to 3000—5000 glucose units. A general discussion and interpretation of these results is deferred, but reference may be made to a preliminary statement of the facts recorded by one of us (Haworth, *Monatsh.*, 1936, **69**, 314).

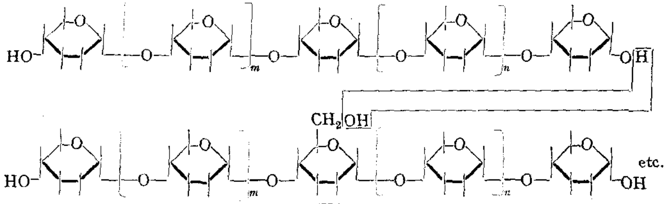
It is significant that from the purified methylated glycogen which had been exhaustively methylated we were able to isolate an amount of dimethyl glucose which is about equivalent to that of the tetramethyl glucose isolated as the end group. Despite every effort to effect

complete methylation of the available hydroxyl groups a very small proportion may escape protection. Methylated glycogen is not of such a nature that it can be purified as rigidly as a substance which is capable of recrystallisation. The origin of the dimethyl glucose may therefore be adventitious. The alternative view, however, has been advanced in our earlier paper on methylated xylan (Haworth, Hirst, and Oliver, J., 1934, 1917). In the latter paper various hypotheses were suggested which apply equally to other polysaccharides which we have investigated and these may again be expressed and emphasised in relation to both glycogen and starch.

On the interpretation suggested in the xylan paper glycogen is represented as groups of 18 (and alternatively of 12) α-glucopyranose units linked at positions 1 and 4 (I) in the form of chains which are themselves joined by a type of union which links the reducing end of one chain with a hydroxyl of an adjoining chain. This occurs through a hydroxyl group, other than that at 1 and 4, of a non-terminal glucose residue. This glucose residue would therefore be united at three points of its ring with adjoining glucose members, leaving *only two exposed hydroxyl groups, which appear therefore as a dimethyl glucose member* in the methylated glycogen. This conception is expressed by (II) and diagrammatically by the laminated formula (III), which are similar to those given by Haworth, Hirst, and Oliver (*loc. cit.*).

(I.) 


(III.)



(II.)

The expression (III) reproduces formula (I) as the line ⟶, and the arrow head gives *the position of the reducing member which engages an adjoining chain. This indicates the linking of consecutive* chains, whether in the manner of an ordinary covalency bond produced by dehydration, or by a co-ordinated or hydroxyl bond connecting the potential reducing end of one chain with another glucose unit of a succeeding chain. At this stage it is not possible to present a precise picture of the nature of this bond or of the position of the intermediate glucose unit involved in this union, but further experiments may make this clear. *Until the orientation of the groups in the dimethyl glucose fragment*, both from glycogen and from starch, has been decided, this and other questions are in abeyance, assuming that the molecular structures (II) and (III) are ultimately found to be the best expression of the experimental facts.

Yet another formulation which must equally be considered is that glycogen (and starch) *consists of a continuous main chain of* α-glucopyranose units linked through the positions 1 and 4 in the form of a loop and having other glucopyranose residues attached as side chains at intervals. This is merely a special case of the expression (III) and has equally been advanced in the earlier paper (Haworth, Hirst, and Oliver, *loc. cit.*).

Experimental.

Properties of Glycogen.—The specimens of glycogen used in this work were prepared from rabbit's liver and had been subjected to the action of 15% aqueous potassium hydroxide during

the process of isolation. The glycogen was a white powder, soluble in cold water, giving opalescent solutions. Colour with iodine, deep red. Non-reducing towards boiling Fehling's solution. Iodine number (Bergmann and Machemer's method, *Ber.*, 1930, **63**, 316) 4·4. $[\alpha]_D^{22°}$ + 188° in water (*c*, 0·3) (Found : P_2O_5, 0·10; ash on incineration, 1·3%) (all data refer to dry material). By electrodialysis the ash content of the glycogen was reduced to 0·3% without appreciable alteration of the other properties.

Acetylated Glycogen.—Alcohol (1750 c.c.) was added gradually to an aqueous solution (250 c.c.) of glycogen (25 g.). The precipitated glycogen was washed rapidly with alcohol and immediately mixed with pyridine (285 c.c.) and acetic anhydride (250 c.c.). The temperature rose slightly and after an hour the glycogen had dissolved almost entirely. After 3 hours the clear solution was poured into cold water and the glycogen acetate was collected, washed, and dried in the usual way. Yield, 90% of the theoretical. This sample of glycogen acetate was a non-reducing (Fehling's solution) white powder, $[\alpha]_D^{22°}$ + 170° in chloroform (*c*, 1·0) (Found : CH_3·CO, 45%). Attempts to divide the acetate into fractions with different properties were unsuccessful. For example, 20 g. of the acetate, dissolved in chloroform, were fractionally precipitated by light petroleum, giving four fractions (5, 3·5, 3·5, and 8 g.) with identical properties, including specific viscosity (Found : $\eta_{sp.}^{20°}$ 0·10 for a solution in *m*-cresol containing 0·05 g. in 5 c.c.; apparent M.W. 3,000, using Staudinger's formula with $K_m = 10^{-3}$). The acetate gave no colour with iodine, but the glycogen regenerated from the acetate by the action of alkali gave the usual deep red colour. Most of the phosphorus in the original glycogen was removed during the acetylation process, the mean of many concordant estimates on the acetate indicating a phosphorus content (calc. as P_2O_5) of 0·02%. In view of the retention of combined phosphorus during the acetylation of starch it is likely, therefore, that most of the phosphorus present in the original glycogen was contained in the adherent inorganic impurities.

Methylated Glycogen.—Glycogen acetate in portions of 10 g., dissolved in acetone (100 c.c.), was methylated at 55° with methyl sulphate (50 c.c.) and 30% aqueous sodium hydroxide (130 c.c.). The methylated glycogen separated as a solid at the end of the experiment and was immediately remethylated. After eight such treatments it was dissolved in chloroform and on evaporation of the solvent was obtained as a pale yellow glass, which was extracted with boiling ether and triturated with light petroleum. Methylated glycogen (yield, 85% of the theoretical) was then obtained as a fine white powder soluble in cold water and in chloroform, insoluble in hot water. The aqueous solution gave a deep red colour with iodine. $[\alpha]_D^{20°}$ + 209° in chloroform (*c*, 1·0) (Found : OMe, 43·3%). A considerable quantity of methylated glycogen was prepared in this way and subjected to fractional precipitation from chloroform solution by light petroleum. For instance, from 40 g. of methylated glycogen six fractions were obtained weighing severally 2, 4, 15, 10, 7, and 1 g. The first fraction (which contained about 1% of mineral matter) and the last (which was obtained by evaporation of the mother-liquors) were neglected. The other four had identical properties, $[\alpha]_{5780}^{19°}$ + 220° in chloroform (*c*, 1·0); $\eta_{sp.}^{20°}$ 0·10 in *m*-cresol solution (0·04 g. in 5 c.c.) corresponding to a chain length of 13 glucose units, using Staudinger's formula with $K_m = 10^{-3}$. All fractions in cold aqueous solution gave a dark red colour with iodine.

Hydrolysis of Methylated Glycogen.—Powdered methylated glycogen (with the properties of fractions 2—5 referred to above) (20 g.) was boiled for 8 hours with 1·2% methyl-alcoholic hydrogen chloride, the progress of the reaction being followed polarimetrically. When the rotation had diminished to a constant value, the hydrochloric acid was removed by silver carbonate and the neutral solution was evaporated to a thin syrup. This was dissolved in ether, and the filtered solution evaporated under diminished pressure, giving a syrup (A) (22·4 g.), which was fractionally distilled, the distillation being stopped when the refractive index of the distillate had reached $n_D^{16°}$ 1·4580. This fraction (5 g.) was redistilled through a column, giving (B) 1·265 g., bath temp. 108—110°/0·04 mm., $n_D^{16°}$ 1·4480, and (C) 1·378 g., bath temp. 120°/0·04 mm., $n_D^{16°}$ 1·4525. Fractions (B) and (C) were mixed and redistilled, giving (D) 1·153 g., bath temp., 104°/0·01 mm., $n_D^{17°}$ 1·4444, and (E) 0·46 g., $n_D^{18°}$ 1·4555. The remainder of (A) and the still residue from the last distillation were joined and redistilled, giving a distillate (F) and an undistillable portion (3·5 g.). The latter was boiled with 1% methyl-alcoholic hydrogen chloride and the product was isolated as before and distilled, giving a distillate (G) and a small undistillable portion. The latter was again boiled with 1% methyl-alcoholic hydrogen chloride and the product gave on distillation (H) together with an undistillable portion which was now negligible in amount. These complications appear to be due to condensation of trimethyl glucose under the influence of methyl-alcoholic hydrogen chloride rather than to incomplete hydrolysis of the methylated glycogen. Similar phenomena are observed when 2 : 3 : 6-trimethyl glucose is boiled with 1% methyl-alcoholic hydrogen chloride. (F), (G) and (H) were

now joined and fractionally distilled through a column. No material of refractive index less than $n_D^{20°}$ 1·456 was detected and after exhaustive fractionation the following were obtained: (J) 18 g., $n_D^{18°}$ 1·4565, (K) 0·2 g., $n_D^{20°}$ 1·4580, and (L) 1·85 g., bath temp. 170—175°/0·01 mm., $n_D^{20°}$ 1·4710 (Found: OMe, 41·8%).

Fraction (D) consisted entirely of tetramethyl methylglucoside and gave on hydrolysis tetramethyl glucopyranose, m. p. 88°, $[\alpha]_D^{20°}$ + 82° in water (*c*, 1·2) (Found: C, 51·0; H, 8·8; OMe, 51·8. Calc. for $C_{9}H_{18}O_{6}$: C, 50·8; H, 8·5; OMe, 52·5%). Fraction (E) was estimated to contain 0·08 g. of tetramethyl methylglucoside. The total yield was therefore 1·233 g. from 20 g. of methylated glycogen. After correction (addition of 10%) to compensate for experimental losses this amounts to 1·35 g. (6·7%), corresponding to a chain length of 18 units for the methylated glycogen.

Fraction (J) was 2 : 3 : 6-trimethyl methylglucoside. Part of it crystallised, giving 2 : 3 : 6-trimethyl β-methylglucopyranoside, m. p. 58°. On hydrolysis both syrup and crystals gave in good yield 2 : 3 : 6-trimethyl glucose, m. p. 117°.

(L) consisted mainly (85—90%) of dimethyl methylglucoside. The yield of dimethyl methylglucoside was therefore approx. 1·6 g. from 20 g. of methylated glycogen. On oxidation by nitric acid (*d* 1·4) at 90° for 8 hours the dimethyl glucose (1 g.) gave a mixture of acids, which were converted into the methyl esters in the usual way. On distillation a fraction (0·3 g.), b. p. 80°/0·01 mm., $n_D^{24°}$ 1·4360, $[\alpha]_D^{20°}$ + 70° in methyl alcohol (*c*, 1·0), was obtained. This was mainly methyl *d*-dimethoxysuccinate, recognised as the corresponding diamide, m. p. 278° (decomp.), $[\alpha]_{5780}^{20°}$ + 94° in water (*c*, 0·23) (Found: OMe, 34·6. Calc. for $C_{6}H_{12}O_{4}N_{2}$: OMe, 35·2%). A considerable proportion of the dimethyl glucose must therefore be the 2 : 3-derivative, but the yield of oxidation product was not sufficiently high to warrant conclusions concerning the homogeneity of the dimethyl methylglucoside.

Control Experiments.—(1) The whole of the above series of operations was repeated with another sample of rabbit liver glycogen. The acetylated glycogen and methylated glycogen were indistinguishable from the corresponding substances obtained in the experiments previously described. After hydrolysis of the methylated glycogen (20 g.) by 1% methyl-alcoholic hydrogen chloride and exhaustive fractional distillation of the product the following yields were recorded, the identity and purity of the substances being established as described above:

(a) Tetramethyl methylglucoside, 1·25 g. (corrected value, 1·38 g.). Chain length of methylated glycogen, 18 units.

(b) Dimethyl methylglucoside, 1·2 g.

(2) Another portion of the glycogen used in the first control experiment was acetylated and thereafter converted into the methyl derivatives by the method already described with the single exception that in this case no less than thirty successive methylations were given. The purified methylated glycogen thus obtained had $[\alpha]_{5780}^{20°}$ + 223° in chloroform (*c*, 1·0), $\eta_{sp.}^{20°}$ 0·130 in *m*-cresol (0·05 g. in 5 c.c.), corresponding to an apparent chain length 13 (Found: C, 52·9; H, 8·1; OMe, 44·8. Calc. for $C_{9}H_{16}O_{5}$: C, 52·9; H, 7·8; OMe, 45·6%). This methylated glycogen (13 g.) was hydrolysed by boiling 1·2% methyl-alcoholic hydrogen chloride. Fractional distillation of the product gave 0·84 g. of tetramethyl methylglucoside (yield, 6·5%), corresponding, after correction, to a chain length of 17 units for the methylated glycogen. The amount of dimethyl methylglucoside in the hydrolysis product was approx. 0·75 g.

(3) In another series of experiments a sample of the methylated glycogen used in the first control series was hydrolysed by a different method. Finely powdered methylated glycogen (20 g.) was added to cold hydrochloric acid (100 c.c.) which had been saturated at 0° with hydrogen chloride. After 44 hours at 15° the solution was diluted, neutralised with barium carbonate, and evaporated to a volume of 150 c.c. This solution (X) was extracted six times with chloroform and the chloroform (1,000 c.c.) was concentrated to a syrup, which was boiled with 1% methyl-alcoholic hydrogen chloride for 8 hours. The methylglucosides (9 g.) were isolated in the usual way and fractionally distilled, giving finally (a) 0·951 g., bath temp. 132—135°/0·07 mm., $n_D^{20°}$ 1·4420 (Found: OMe, 60·9%), and (b) 0·424 g., bath temp. 143—144°/0·07 mm., $n_D^{22°}$ 1·4490. The remainder consisted entirely of 2 : 3 : 6-trimethyl methylglucoside. (a) and (b) together contained 1·2 g. of tetramethyl methylglucoside. The solution (X) was evaporated to dryness, and the organic material extracted with boiling chloroform and converted into the methylglucosides. Fractional distillation showed that no tetramethyl methylglucoside was present, the material not removed from the aqueous solution by the chloroform extraction being 2 : 3 : 6-trimethyl glucose together with a little dimethyl glucose. The total yield of tetramethyl methylglucoside was therefore 1·2 g. from 20 g. of methylated glycogen (chain length, 20 units). The identity of the products was established by the methods given above.

(4) *Experiments with artificial mixtures.* (a) The efficiency of the fractionating column used in the preceding experiments was tested by distilling through it a mixture of 2 : 3 : 6-trimethyl methylglucoside (3·50 g.) and 2 : 3 : 4 : 6-tetramethyl methylglucoside (0·43 g.). The procedure was exactly similar to that used in the experiments with glycogen and the yield of tetramethyl methylglucoside recovered was 0·395 g. (92%). The quantity used in the control experiment was less than that distilled in the course of the experiments with glycogen and in this respect the test of the apparatus was more stringent. In other experiments it was demonstrated that no tetramethyl methylglucoside escaped during the distillation, since no trace of the latter was detectable in a receiver, cooled in acetone–solid carbon dioxide, placed between the pump and the distillation apparatus.

(b) A set of experiments similar to (a) but commencing with 2 : 3 : 6-trimethyl glucose (5·69 g.) and 2 : 3 : 4 : 6-tetramethyl glucose (0·42 g.) was then carried out. The mixed sugars were transformed into the methylglucosides and the mixture of the latter was distilled through the column. The yield of tetramethyl methylglucoside was 0·40 g. (90% recovery). Here again the choice of small quantities was deliberate in order to test the accuracy of the experimental procedure under the least favourable conditions. There is therefore no possibility of serious experimental loss of tetramethyl glucose at any stage of the work on methylated glycogen.

The University of Birmingham, Edgbaston. [*Received, February 13th, 1937.*]

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130. *The Influence of Solvents and of other Factors on the Rotation of Optically Active Compounds. Part XXXIV.* The Influence of Water and of Deuterium Oxide.*

By Charles Buchanan.

When these experiments were started, the only relevant publication was Pascu's observation (*J. Amer. Chem. Soc.*, 1934, **56**, 745) that the rotation at equilibrium of α-*d*-glucose in deuterium oxide was $[\alpha]_D^{20^\circ}$ $+52·14°$ as against $+52·06°$ in water. Erlenmeyer and Schenkel (*Helv. Chim. Acta*, 1936, **19**, 1381) have since shown that phenylbenzylmethyl*iso*propylammonium nitrate gives a small difference in rotation in water and in heavy water. From Pascu's observation it appeared that any effect would probably be small, so methyl *d*-tartrate was first chosen for examination, since the rotation of the alkyl tartrates is very sensitive to changes of solvent; also, since the methyl ester is solid, it could be more readily recovered from solution if necessary. It was recognised that any rotation difference with this compound might be due either to hydrogen interchange or to solvent effect, or both, but it was thought that some idea of the magnitude of the rotation changes to be expected with heavy water might be obtained.

The rotation of methyl *d*-tartrate in deuterium oxide (99%) is less than in water for the same concentration in g. per 100 g. of solution. The rotations were examined at different temperatures, and from the temperature–rotation curves by interpolation, we find :

In deuterium oxide, $p = 24·84$: $[\alpha]_D^{20^\circ} = +18·10°$; $[\alpha]_{5461}^{20^\circ} = +20·35°$.
In water, $p = 24·89$: $[\alpha]_D^{20^\circ} = +18·65°$; $[\alpha]_{5461}^{20^\circ} = +21·10°$.

The differences, for $[\alpha]_D$ 0·55°, and for $[\alpha]_{5461}$ 0·75°, are greater than the probable experimental error. If, however, the rotations for the same concentration in g. per 100 c.c. had been compared, the difference would be much less, and probably not more than the experimental error. A better comparison would be between solutions containing the same molecular proportion of solvent to methyl tartrate; for such solutions, $p = 24·84$ in deuterium oxide would correspond to $p = 26·87$ in water, and for the latter solution it can be calculated from Patterson's data (J., 1904, **85**, 1149) that $[\alpha]_D^{20^\circ} = +18·30°$. The difference would thus be 0·20°, which is about the probable experimental error. There is no appreciable difference in the shape of the temperature–rotation curves, each of which shows a maximum at about 25°.

An attempt was made to find if methyl *d*-tartrate, which had been dissolved in deuterium

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oxide, and presumably had exchanged two hydrogens for deuterium, would show any difference in rotation when recovered from the solvent and examined in an indifferent solvent, as has been observed by Erlenmeyer and Schenkel (*Helv. Chim. Acta*, **1936**, **19**, 1199) for *l*-mandelic and *l*-atrolactinic acids. No such difference in rotation could be detected.

Methyl *d*-dimethoxysuccinate was next examined, since it contains no replaceable hydrogen atoms. No difference was observed in the rotation of this substance for solutions having $p = 20$ in water and in deuterium oxide.

Nicotine was also examined, as its rotation is considerably influenced by solution in water. For solutions having $p = 10$, nicotine has a somewhat higher rotation in deuterium oxide, $[\alpha]^{20°}_{5461}$ $-96·28°$, than in water, $[\alpha]^{20°}_{5461}$ $-95·05°$. As the specific rotation of nicotine at this concentration is practically unaltered by small changes in concentration (cf. Landolt, *Annalen*, 1877, **189**, 322; Tate and Warren, *J. Soc. Chem. Ind.*, 1937, **56**, 39), the same difference would be obtained by comparing solutions of the same concentration in g. per 100 c.c. Here, again, there is no appreciable difference in the shape of the temperature–rotation curves.

It was observed, incidentally, that there is a distinct difference in the solubility of nicotine in deuterium oxide and in water: a solution of nicotine in deuterium oxide, $p = 10·09$, on heating becomes turbid at 60·5°; nicotine in water, $p = 10·22$, becomes turbid at 73·5°.

EXPERIMENTAL.

The water and the deuterium oxide (99%) were boiled gently for a short time, to expel the bulk of the dissolved air, before being used for the solutions. The rotations were examined in a 40 mm. tube.

Methyl d-*Tartrate*.—(i) *In water*, $p = 24·89$. Densities determined :

t	11°	26°	36°	49·5°	69°	86°	97·5°
d	1·0809	1·0746	1·0693	1·0617	1·0489	1·0361	1·0272

t.	d.	α_D.	α_{5461}.	$[\alpha]_D$.	$[\alpha]_{5461}$.
0°	1·0848	+2·00°	+2·24°	+18·52°	+20·74°
17	1·0780	1·99	2·27	18·54	21·15
33·5	1·0706	1·955	2·26	18·33	21·20
50	1·0616	1·915	2·15	18·12	20·34
64·5	1·0523	1·85	2·09	17·66	19·95
80·5	1·0407	1·74	2·00	16·79	19·30
94	1·0299	1·67	1·87	16·29	18·24
17	after cooling	2·01	2·27	18·72	21·15

The above values for $[\alpha]_D$ and the corresponding values given by Patterson (*loc. cit.*) lie on the same curve.

(ii) *In deuterium oxide*, $p = 24·84$. Densities determined :

t	9°	21·5°	31°	44·5°	51·4°	63°	73·5°	94°
d	1·1742	1·1692	1·1639	1·1560	1·1513	1·1427	1·1344	1·1174

t.	d.	α_D.	α_{5461}.	$[\alpha]_D$.	$[\alpha]_{5461}$.
0°	1·1770	+2·115°	+2·37°	+18·09°	+20·27°
25·5	1·1670	2·09	2·36	18·14	20·35
37·8	1·1602		2·33		20·08
47	1·1542	1·99	2·28	17·35	19·88
61°	1·1440	1·95	2·185	17·16	19·22
74·5	1·1336	1·86	2·09	16·16	18·56
25·5	after cooling		2·37		

4 G. of methyl tartrate were dissolved in 4 c.c. of water; 200 c.c. of benzene, dried over freshly heated sodium sulphate, were added, and the mixture shaken. Sodium sulphate in excess was added to take up the water, and, after standing over-night in a desiccator, the solution was filtered, the benzene distilled off, and used to extract the sodium sulphate again. The bulk of the benzene was finally distilled off, freshly dried light petroleum (b. p. 60—80°) (30 c.c.) added, and the solution allowed to crystallise. This was repeated, deuterium oxide being used instead of water, and the rotation of the two samples was examined in freshly distilled nitrobenzene.

Ester from H_2O; p = 8·2174.

t.	d.	α_{5461}.*	$[\alpha]_{5461}$.
0°	1·2307	+3·39°	+21·00°
21	1·2110	3·45	21·72

Ester from D_2O; p = 8·2056.

t.	d.	α_{5461}.*	$[\alpha]_{5461}$.
0°	1·2310	+3·385°	+20·94°
21	1·2116	3·45	21·69

* l = 160 mm.

Methyl d-*Dimethoxysuccinate*.—(i) *In water*, p = 19·872. Densities determined :

t	11°	21°	36·8°	50·5°	67°
d	1·0403	1·0365	1·0293	1·0214	1·0108

t.	d.	α_D.	α_{5461}.	$[\alpha]_D$.	$[\alpha]_{5461}$.
0°	1·0438	+6·93°	+8·15°	+83·52°	+98·23°
18	1·0375	6·59	7·75	79·91	93·97
38	1·0281	6·22	7·30	76·11	89·32
58	1·0165°	5·87	6·90	72·65	85·39
78·5	1·0027	5·55	6·51	69·63	81·68
18·5			7·745		

This was repeated in order to obtain some idea of the experimental error. p = 20·147. Densities determined :

t	11°	33°	49·5°	77·5°
d	1·0413	1·0322	1·0228	1·0040

0	1·0448	+7·07	+8·28	+83·81	+98·15
21	1·0376	6·60	7·78	78·93	93·04
37	1·0300	6·33	7·45	76·26	89·75
61	1·0160	5·91	6·97	72·18	85·13
78·5	1·0040	5·63	6·62	69·58	81·82
18·5	after cooling	—	7·89		

(ii) *In deuterium oxide*, p = 20·013. Densities determined :

t	11·8°	23°	36·5°	50°	66·7°	81·6°
d	1·1321	1·1272	1·1203	1·1123	1·1009	1·0889

0	1·1340	+7·56	+8·90	+83·28	+98·04
20	1·1282	7·16	8·42	79·29	93·23
40	1·1180	6·78	7·96	75·76	88·94
59·5	1·1054	6·43	7·545	72·66	85·26
81·8	1·0888	6·05	7·12	69·41	81·68

After cooling : $\alpha_{5461}^{20°}$ = 8·45°; after standing over-night : $\alpha_{5461}^{17°}$ = 8·53°.

Nicotine.—(i) *In water*, p = 10·371. Densities determined :

t	9·5°	22·6°	34·2°	43·2°	53°	65°
d	1·0084	1·0046	1·0005	0·9965	0·9914	0·9845

t.	d.	α_D.	α_{5461}.	$[\alpha]_D$.	$[\alpha]_{5461}$.
0°	1·0100	−3·10°	−3·75°	−73·99°	−89·50°
20	1·0053	3·26	3·97	78·17	95·20
39	0·9982	3·48	4·19	84·04	101·20
59·5	0·9878	3·65	4·405	89·07	107·50

In water, p = 10·222. Densities determined :

t	10°	20·1°	29·6°	39·9°	49·5°	60°
d	1·0078	1·0051	1·0020	0·9979	0·9934	0·9875

0	1·0098	−3·05	−3·68	−73·87	−89·12
20·5	1·0050	3·20	3·90	77·87	94·90
39·2	0·9980	3·41	4·13	83·56	101·20
59	0·9878	3·59	4·33	88·88	107·20

(ii) *In deuterium oxide*, p = 10·09. Densities determined :

t	13°	21·5°	30°	41°	52°	59·9°
d	1·1033	1·1012	1·0982	1·0933	1·0876	1·0832

0	1·1056	−3·33	−4·03	−74·62	−90·31
20	1·1014	3·57	4·28	80·31	96·28
39·2	1·0940	3·75	4·52	84·93	102·36
59	1·0836	3·95	4·80	90·32	109·75

SUMMARY.

The optical rotation of solutions in water and in deuterium oxide (99%) of (I) methyl *d*-tartrate, (II) methyl *d*-dimethoxysuccinate, and (III) *l*-nicotine, has been examined for two colours of light and at different temperatures, with the following results:

(I) Concentration, $p = 25$; specific rotation about 3% lower in deuterium oxide. (II) Concentration, $p = 20$; specifical rotations identical. (III) Concentration, $p = 10$; specific rotation about 1% higher in deuterium oxide.

Nicotine was found to be less soluble in deuterium oxide than in water at 60·5°.

The author wishes to thank Professor T. S. Patterson, at whose suggestion this work was undertaken, for advice during its progress.

THE UNIVERSITY, GLASGOW. [*Received, February 25th*, 1937.]

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131. *Alkaloids of Senecio. Part III. Jacobine, Jacodine, and Jaconine.*

By G. BARGER and J. J. BLACKIE.

THE alkaloidal content of *Senecio Jacobæa* L., the common ragwort, was first closely examined by Manske (*Canadian J. Res.*, 1931, **5**, 651), who described a crystalline alkaloid, jacobine, to which he assigned the formula $C_{18}H_{23}O_5N$; on hydrolysis he obtained retronecine, $C_8H_{13}O_2N$, and jaconecic acid, for which the formula $C_{10}H_{16}O_6$ was given with reserve. If all three formulæ were correct, hydrolysis would involve the addition of three molecules of water, whereas in the *Senecio* alkaloids hitherto examined, at most two have been required, one for the ester group and one for a lactone group in the acidic portion of the molecule. Manske's analytical results, moreover, do not agree closely with the formulæ assigned. Some years ago we found in *S. Jacobæa* two alkaloids which differ in rotation (not determined by Manske) but not much in solubility. One of them has since been isolated by Hosking and Brandt (*New Zealand J. Sci. Tech.*, 1936, **17**, 638), who assigned to it the formula $C_{18}H_{25}O_6N$ but no name. Lately, from material collected in August (instead of June and July as before), we obtained only one alkaloid, apparently identical with that of Hosking and Brandt. For the sake of simplicity we suggest the retention of Manske's name jacobine, for it is certainly the principal alkaloid in the plant. We have obtained analyses for it and for its fission products in agreement with the equation

$$C_{18}H_{25}O_6N + 2H_2O = C_8H_{13}O_2N + C_{10}H_{16}O_6$$

The basic fission product is, as Manske found, retronecine; the acid is isomeric with retronecic and isatinecic acids (cf. Blackie, *Pharm. J.*, 1937, **138**, 102) from South African species of *Senecio*, but whilst the latter acids contain two *C*-methyl groups and are cyclic dihydroxy-compounds, jaconecic acid contains three (or four?) *C*-methyl groups and is most likely an acyclic hydroxy-ketonic acid. Senecic acid ($C_{10}H_{14}O_4$, from senecionine) is an acyclic unsaturated lactonic acid.

In our earlier material jacobine was mixed with an alkaloid $C_{18}H_{25}O_5N$ (isomeric with senecionine and squalidine; J., 1936, 743) having a higher lævorotation, a smaller solubility in ethyl acetate, and forming a nitrate more soluble in alcohol than that of jacobine; for this alkaloid we suggest the name *jacodine*. Like senecionine, it is unsaturated, but its lævorotation and solubility in alcohol are much greater than those of senecionine. Evidently Manske's alkaloid was not pure and his analytical results are explained by a contamination with jacodine, which we found very difficult to separate from jacobine.

From the mother-liquors of jacobine and jacodine, obtained from material collected in July, 1934, we isolated a small quantity of a base, $C_{18}H_{25}O_8N,H_2O$, which is very soluble in alcohol, and may be called *jaconine*. We have failed to isolate it from later material, from which jacodine also was absent.

On account of the occurrence of *Senecio* poisoning of cattle in New Zealand (Winton

disease), we examined a supply of *S. Jacobæa* collected there through the kindness of Dr. B. C. Aston, chief chemist of the Department of Agriculture, Wellington; for his help in this matter we tender him our hearty thanks. The alkaloidal content was the same (0·06%) as in the Scottish plant, and the same mixture (of jacobine and jacodine) appeared to be present. The greater incidence of poisoning in New Zealand is probably due to a greater abundance of *Senecio* in the pasture.

Jacobine is also the principal alkaloid in *S. cineraria*, D.C., a Mediterranean plant, which has established itself on the coast near Dublin, whence our material was obtained. Although very different in appearance from *S. Jacobæa*, *S. cineraria* seems to be a closely related species, for the two hybridize in Ireland (Colgan, "Flora of the County Dublin," Dublin, 1904, p. 112); such biological relationship is in accordance with the presence of the same alkaloid in both species. *S. cineraria* probably contains a small amount of another alkaloid with a lower rotation. Manske (*Canadian J. Res.*, 1936, **14**, 6), working with very little material, found this species practically devoid of alkaloid. We suggest that aureine (from *S. aureus* L.), described in the same paper, may be identical with senecionine, which, as we have previously shown (J., 1936, 743), Manske failed to obtain pure. The optical rotation of aureine (not recorded) would help to settle this point. We further suggest that the acid $C_{10}H_{16}O_4$, found by Manske in *S. mikanoides* (Walp) Otto, m. p. 64°, is in reality dimethylacrylic acid, previously isolated from *S. kæmpferi* D.C. by Shimoyama (*Apoth. Ztg.*, 1892, **7**, 453) and identified as such by Asahina (*Arch. Pharm.*, 1913, **251**, 355).

Experimental.

S. Jacobæa.—7 Kg. (dry), collected in June, 1934, yielded 2·1 g. (0·03%); 29 kg. (July, 1934), 16·6 g. (0·06%); 36 kg. (August, 1935), 18·19 g. (0·05%); and 3·3 kg., from New Zealand, 1·91 g. (0·06%)

S. cineraria.—2 Kg., collected at the end of June, 1936, near Dublin, yielded 1·05 g. (0·05%). The material was extracted by the method previously described (J., 1936, 743). Both batches in 1934 yielded a mixture of jacobine and jacodine; that collected in June had $[\alpha]_D^{16°}$ − 62·6°; that collected in July had $[\alpha]_D^{16°}$ − 84·2°; both melted at 212°; the former mixture gave C, 61·8; H, 7·3%, approximating fairly closely to $C_{18}H_{25}O_6N$, but, as indicated by the rotation, the latter mixture contained a considerable proportion of jacodine and it gave analytical results not in agreement with any simple formula. Crystallisation from alcohol had little effect in separating the second mixture, as shown by the rotation of the fractions; nor had a fractional extraction with hydrochloric acid from chloroform solution. Crystallisation of the nitrates from absolute alcohol was rather more effective; the least soluble nitrate yielded a base with C, 62·1; H, 6·9% (approximating to $C_{18}H_{25}O_5N$), but not yet quite pure.

Jacobine.—The alkaloid was only obtained pure from the 1935 and 1936 material. It crystallised from absolute alcohol in nacreous diamond-shaped plates, m. p. 219°; the alkaloid from *S. Jacobæa* had $[\alpha]_D^{17°}$ − 46·3° (*c*, 1·51 in chloroform), and that from *S. cineraria*, $[\alpha]_D^{17°}$ − 30·5° (*c*, 1·44 in chloroform); the lower value is probably due to contamination with another alkaloid of lower rotation. Jacobine is more soluble in absolute alcohol than senecionine (*ca.* 1 in 110), very soluble in chloroform, slightly in ether, and moderately readily in ethyl acetate (about twice as soluble as jacodine) (Found for alkaloid from *S. Jacobæa*: C, 62·1, 62·1; H, 7·1, 7·2; N, 4·1; for alkaloid from *S. cineraria*: C, 61·8; H, 7·2; N, 4·3. Calc. for $C_{18}H_{25}O_6N$: C, 61·5; H, 7·2; N, 4·0%). Jacobine contains two active hydrogen atoms (Found according to Zerewitinoff, 1·76, 1·71).

Jacobine nitrate, prepared by dissolving the base in the calculated quantity of 0·1*N*-acid and evaporating the solution, forms prisms from water and rhombic plates from alcohol, m. p. 234°, $[\alpha]_D^{17°}$ − 28·6° (*c*, 1·68 in water) (Found for *S. Jacobæa*: C, 52·4, 52·6; H, 6·3, 6·1; for *S. cineraria*: C, 52·2, 52·1; H, 6·5, 6·4. $C_{18}H_{25}O_6N,HNO_3$ requires C, 52·2; H, 6·3%). The picrate is very soluble in cold water and crystallises from alcohol in needles, m. p. 180°. The methiodide forms stout prisms, m. p. 255°, from alcohol.

Hydrolysis (for method, see Part I, J., 1935, 13). Retronecine was obtained both from *S. Jacobæa* and from *S. cineraria*, m. p. 119° alone or with retronecine ($[\alpha]_D$ + 50·8°) from *S. retrorsus*; $[\alpha]_D$ + 50·5°, + 49·9° respectively.

Jaconecic Acid.—Like other acids from *Senecio* alkaloids, this acid was only obtained pure with difficulty, particularly from our earlier mixtures. On prolonged standing in a desiccator the syrup partly crystallised; an impurity could then be removed with *dry* ether, and the

residue could be recrystallised from a concentrated solution in acetone by the addition of *dry* ether. From the pure alkaloid the acid was more readily obtained crystalline. It separated from dry ether in fine needles, m. p. 182° (Hosking and Brandt give m. p. 181° but no analysis); $[\alpha]_D^{18°}$ + 31·7° (Found: C, 51·4; H, 7·1. Calc. for $C_{10}H_{16}O_6$: C, 51·7; H, 6·9%). Jaconecic acid from *S. cineraria* melted at 181°, alone or mixed with authentic material. *C*-Methyl estimation by Dr. H. Roth: Found, 3·10, 3·17.

Jacodine.—We have obtained this alkaloid analytically but perhaps not yet optically pure. The more soluble fraction of the mixed nitrates had a much higher lævorotation than jacobine nitrate; m. p. 215°, $[\alpha]_D^{17°}$ − 77·4° (*c*, 1·33 in water). From this nitrate we obtained a *base*, which was recrystallised from ethyl acetate, in which it was less soluble than jacobine; it formed long plates pointed at both ends, m. p. 217°, $[\alpha]_D^{17°}$ − 109·6° (*c*, 1·48 in chloroform) (Found: C, 64·3; H, 7·2; N, 4·3. $C_{18}H_{25}O_5N$ requires C, 64·4; H, 7·2; N, 4·3%). The picrate was very little soluble in water and formed needles, m. p. 171°, from alcohol.

Hydrolysis of the base yielded retronecine, m. p. 119° (not depressed by an authentic specimen), and an acid, which formed sphæro-crystals and needles, m. p. 136—137°, from chloroform (Found: equiv., 116. Calc. for a dibasic acid $C_{10}H_{16}O_5$: equiv. 108). The small amount of the material did not permit of complete purification.

Jaconine separated from the concentrated mother-liquors of the two previous alkaloids in prisms, m. p. 146°, very soluble in alcohol, moderately soluble in ethyl acetate, and somewhat soluble in water. The amount obtained was very small (Found for air-dried material purified from alcohol: C, 54·4; H, 6·9; N, 3·5; loss on drying at 50° in a high vacuum, 4·5. Found for anhydrous material: C, 56·8; H, 6·4. $C_{18}H_{25}O_8N,H_2O$ requires C, 53·9; H, 6·8; N, 3·5; H_2O, 4·5%. $C_{18}H_{25}O_8N$ requires C, 56·4; H, 6·6%).

In spite of the high oxygen content the alkaloid distilled at 180°/0·01 mm. without *apparent* decomposition; the vitreous solid crystallised in flat prisms when the tube was heated in a water-bath. The vapours evolved on heating with zinc dust coloured pine-wood red. It is not certain whether the distillate was identical with the material as first crystallised.

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132. *Chemiluminescent Organic Compounds. Part IV. Amino- and Hydrazino-*cyclo*phthalhydrazides and their Relative Luminescent Power.*

By H. D. K. Drew and F. H. Pearman.

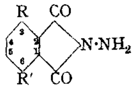
The amino-substituted phthalaz-1 : 4-diones (particularly the 5-amino-derivative) luminesce more strongly than the other known members of the series. A number of amino- and hydrazino-substituted diones, and their derivatives containing acetyl and methyl groups, are now described, together with some of their 5-ring isomerides (*N*-amino-imides). The last are non-luminescent, but several of the new diones are comparable, as regards luminescent power, with the 5-amino-dione at laboratory temperature and somewhat superior to it at 100°.

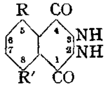
Methylation of 3-aminophthalimide with methyl sulphate gave 3-*methylaminophthalimide*, but with methyl iodide the chief product was the *methiodide* of N-*methyl*-3-*dimethylaminophthalimide*, from which the molecule of methyl iodide could not be eliminated. 3-Methylaminophthalimide gave N-*amino*-3-*methylaminophthalimide* (I; R = CH_3·NH, R′ = H) with 1 mol. of aqueous hydrazine hydrate, and 5-methylaminophthalaz-1 : 4-dione (II; R = CH_3·NH, R′ = H) with 3 mols. of hydrazine hydrate; (I) is transformed above its melting point into (II).

3 : 6-*Diaminophthalimide*, which occurs in a red and a golden-brown form, was obtained by heating 3 : 6-dichlorophthalimide or 3 : 6-dichlorophthalic anhydride with ammonia under pressure in presence of cuprous iodide. This phthalimide is changed into red 3 : 6-*diamino*-N-*aminophthalimide* (I; R = R′ = NH_2) with excess of aqueous hydrazine at 90°, but into yellow 5 : 8-*diaminophthalaz*-1 : 4-*dione* (II; R = R′ = NH_2) with hydrazine

hydrate at 120°. 3 : 6-Diamino-*N*-aminophthalimide does not react with hydrazine hydrate at room temperature, although *N-amino-3 : 6-diacetamidophthalimide* reacts at once. 3 : 6-Dichloro-*N*-aminophthalimide in these circumstances forms the open-chain dihydrazide, which re-forms the 5-ring compound at room temperature in water or when acidified but closes to the 6-ring *cyclo*-hydrazide at 120° (this vol., p. 26). These cases illustrate the effect of temperature on the ring closure of the open-chain hydrazides. 3 : 6-Diaminophthalic acid was not obtained pure, but 3 : *6-diacetamidophthalic anhydride* was prepared.

4 : *5-Dichlorophthalimide* could not be converted into 4 : 5-diaminophthalimide with ammonia and cuprous iodide, but 6 : 7-dichlorophthalaz-1 : 4-dione was changed by these reagents into the required 6 : *7-diaminophthalaz-*1 : *4-dione*, which crystallised as a *dihydrate*.


(I.)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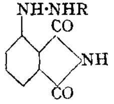
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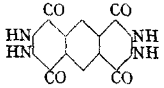
(IV.)

Diazotisation and reduction of 3-aminophthalimide gave *sodium phthalimide-3-hydrazine-β-sulphonate* (III, R = SO_3Na) and this was changed by mineral acid into *3-hydrazinophthalimide* (III, R = H), which occurs in a yellow and an orange form having identical chemical properties but differing in melting point. Similar pairs of forms occur among other substituted phthalimides (Pratt and Perkins, *J. Amer. Chem. Soc.*, 1918, **40**, 203; Chattaway, J., 1911, 1915); they are not accountable by reference to lactam-lactim tautomerism, since they arise also in cases where the hydrogen of the imino-group is substituted. Alcoholic hydrazine hydrate converted 3-hydrazinophthalimide and the above sulphonate into orange *N-amino-3-hydrazinophthalimide* (I; R = $NH{\cdot}NH_2$, R′ = H) and *sodium N-aminophthalimide-3-hydrazine-β-sulphonate* (I; R = $NH{\cdot}NH{\cdot}SO_3Na$, R′ = H) respectively, and excess of aqueous hydrazine hydrate converted them into white *5-hydrazinophthalaz-*1 : *4-dione* (II; R = $NH{\cdot}NH_2$, R′ = H) and *sodium phthalaz-*1 : *4-dione-5-hydrazine-β-sulphonate* (II; R = $NH{\cdot}NH{\cdot}SO_3Na$, R′ = H) respectively.

*Pyromellitaz-*1 : 4 : 6 : *9-tetraone* (IV), a bis*cyclo*phthalhydrazide of novel type, was prepared from pyromellitic anhydride and hydrazine. It shows a powerful yellow chemiluminescence with alkaline oxidising agents. Its amino-derivatives and others are being examined.

It was noticed throughout that fluorescence occurred in the phthalimides and *cyclo*-hydrazides containing an amino-group in an *o*-position to the junction of the rings, but not in those containing an amino-group in the *m*-position. The *N*-aminophthalimides derived from fluorescent phthalimides were non-fluorescent; this is not due to the removal of the imide hydrogen, but is an effect of the *N*-amino-group itself, since fluorescence persists in the *N*-methyl- and *N*-phenyl-phthalimides.

Luminescent Power.—The substances described in this and in our previous paper (J., 1937, 26) were tested for chemiluminescence by oxidation, in presence of aqueous sodium hydroxide or ammonia, with hydrogen peroxide and other oxidising agents, both alone and with hæmoglobin or a copper salt as catalyst. Only the phthalaz-1 : 4-diones showed chemiluminescence, the 5-ring compounds giving no visible light in any instance. The open-chain hydrazides glow only when transformation into 6-ring hydrazides has taken place.

By means of a Karrer–Poritsky low-brightness optical photometer the chemiluminescence of the diones was compared at 18° and at 100°. The optimum conditions for 5-aminophthalaz-1 : 4-dione were first found and the other diones were tested with the same molecular proportions of reagents. The table shows the qualitative order of brightness observed under the two sets of conditions, the ascending numbers indicating the places of the substances in decreasing order of brightness.

Phthalaz-1 : 4-dione.	Colour of *light* emitted.	Order of brightness. At 18° (*in presence of* hæmoglobin).	At 100° (without catalyst).
5-Amino-	blue	1	4
5-Methylamino-	greenish-blue	2	2
5 : 8-Diacetamido-	greenish	3	1
5-Hydroxy-	bluish-violet	4	3
5-Hydrazino-	blue	5	7
5-Acetamido-	greenish-blue	7	6
6-Amino-	blue	8	8
5 : 8-Dichloro-	bluish-violet	9	9
5-Chloro-	,,	10	11
6-Acetamido-	blue	11	13
†5 : 8-Diamino-	whitish-blue	12	12
5-Benzamido-	blue	13	14
5-Hydrazine-β-sulphonate	whitish-blue	14	18
Phthalaz-1 : 4-dione	,,	15	10
†6 : 7-Diamino-	bluish-violet	16	16
†5-Nitro-	whitish-yellow	17	15
6 : 7-Dichloro-	bluish-violet	18	17
†6-Nitro-	whitish-yellow	19	19
Pyromellitaz-1 : 4 : 6 : 9-tetraone	yellow	6	5

† *indicates that the observed brightness was too low owing to internal absorption* (coloured solution).

The observations at 18° were made on 1 c.c. of 0·04*M*-solution of the dione containing 12 molecular proportions of sodium hydroxide, to which were added 4 drops of aqueous hydrogen peroxide (6%) and 6 drops of hæmoglobin solution (1%) in 0·1*N*-sodium hydroxide; those at 100° were made in the same manner, but the hæmoglobin was omitted.

The points which emerge from the comparisons are: (1) Negative (*op*-directing) groups (NH_2, NH·Me, OH, NH·NH_2, and, to a lesser extent, Cl) cause increased light emission in the visible region; whereas positive (*m*-directing) groups (NO_2, and such groups as CO·CH_3, COPh, and SO_3Na substituted in side chains) tend to have the opposite or at least a much weaker effect.

(2) Substitution of favourable groups in the 5- and 8-positions has a much greater effect than substitution in the 6- and 7-positions.

(3) Substitution in the 5- and 8-positions of two favourable groups usually produces a greater effect than substitution of one such group only (5 : 8-diaminophthalaz-1 : 4-dione appears to be an exception, but its red solution is strongly absorbent and it should probably be placed near the top of the list).

(4) The emitted visible light is changed in colour and greatly increased in intensity when phthalaz-1 : 4-dione is converted into pyromellitaz-1 : 4 : 6 : 9-tetraone, which contains two hydrazide rings.

(5) The order of brightness is changed with increase of temperature.

Preliminary measurements with seven of the diones indicated that maximum luminescence was obtained with 10—16 mols. of sodium hydroxide per mol. of dione, the quantity varying with the nature of the dione but being usually about 12 mols.; 4—5 mols. of hydrogen peroxide were required for maximum brightness, further increase producing no effect. With these proportions of dione and sodium hydroxide, the effect of dilution over the range 0·02 to 0·08*M* was small, equal volumes of the solutions containing the same amounts of hydrogen peroxide and hæmoglobin being employed for the comparison.

EXPERIMENTAL.

N-*Methyl*-3-*dimethylaminophthalimide Methiodide*.—3-Aminophthalimide (1 g.), methyl iodide (4 g.; 4 mols.), and 96% methyl alcohol (15 c.c.) were heated in a sealed tube at 120—130° for 8 hours; the crystals deposited were filtered off (a further crop was obtained from the filtrate; total yield, 0·9 g.) and recrystallised from methyl alcohol. The *methiodide* formed colourless tetragonal plates, m. p. 204° (decomp.), very soluble in water and alcohol (Found: C, 42·0; H, 4·5. $C_{12}H_{15}O_2N_2I$ requires C, 41·8; H, 4·35%). Silver nitrate precipitated silver iodide, and aqueous silver oxide gave also deliquescent colourless needles of the base. Sublimation, boiling with quinoline or with sodium ethoxide in ethyl alcohol, or heating with ammonia under pressure failed to remove methyl iodide. When 1, 2, or 3 mols. of methyl iodide were employed

in the preparation, mixtures of 3-methylaminophthalimide (below), the above methiodide, and unchanged material were obtained, indicating that the imide ring becomes methylated only after dimethylation of the amino-group and formation of the methiodide.

3-Methylaminophthalimide.—3-Aminophthalimide (2 g.) and methyl sulphate (3 c.c.) were heated at 120—130° for ½ hour under reflux; the brown fluid was stirred into water (200 c.c.), and the yellow powder obtained recrystallised from boiling water (500 c.c.). The *substance* (1 g.) formed long, deep yellow needles, m. p. 218° (Found: C, 61·1; H, 4·5; N, 16·0. $C_9H_8O_2N_2$ requires C, 61·3; H, 4·5; N, 15·9%). Solutions in boiling water or alcohol had a deep green fluorescence, but in benzene or acetone the fluorescence was bluish. A nitroso-derivative was obtained, in colourless needles, by the action of nitrous acid on a solution in hydrochloric acid. The compound is soluble in cold alkalis. The 3-N-*acetyl* derivative was obtained, by boiling it with excess of acetic anhydride in presence of a trace of concentrated sulphuric acid, in pale buff prisms (from glacial acetic acid), m. p. 285° (decomp.); its solutions were only weakly fluorescent (Found: C, 60·4; H, 4·9. $C_{11}H_{10}O_3N_2$ requires C, 60·55; H, 4·6%).

N-*Amino-3-methylaminophthalimide.*—A mixture of 3-methylaminophthalimide (1·2 g.) and hydrazine hydrate (0·36 g.; 1 mol.) in water (20 c.c.) was refluxed for 1 hour; the crystals produced were freed from traces of the isomeric *cyclo*-phthalhydrazide by washing with 2% sodium hydroxide solution. The *amino-phthalimide* (1·1 g.) formed yellow prismatic needles (Found: C, 56·6; H, 4·95. $C_9H_9O_2N_3$ requires C, 56·55; H, 4·7%); it melted at 194°, but at higher temperatures transformation into the *cyclo*hydrazide occurred; its solutions were not fluorescent.

5-Methylaminophthalaz-1 : 4-*dione.*—3-Methylaminophthalimide (1·2 g.) and hydrazine hydrate (1·1 g.; 3 mols.) were refluxed for 1 hour; the product was present partly as its hydrazine salt, which was hydrolysed by water. The phthalazdione formed cream-coloured microcrystals, m. p. 331° (decomp.); Gleu and Pfannstiel (*J. pr. Chem.*, 1936, **146**, 137) gave m. p. 310—325° (decomp.). It was little soluble in ordinary solvents but dissolved in alkalis (violet fluorescence) or in concentrated hydrochloric acid (Found: C, 56·7; H, 4·9. Calc. for $C_9H_9O_2N_3$: C, 56·55; H, 4·7%). Its sodium salt was decomposed by carbon dioxide, and it readily yielded a nitroso-compound (buff needles). The 5-N-*acetyl* derivative, prepared by heating the 3-*N*-acetyl derivative of 3-*N*-methylaminophthalimide and hydrazine hydrate (1 mol.) in water, formed small, pointed, buff needles (from water), m. p. 329° (decomp.), not fluorescent in neutral solutions (Found: N, 18·2. $C_{11}H_{11}O_3N_3$ requires N, 18·0%).

3 : 6-*Diaminophthalimide.*—(a) A mixture of 3 : 6-dichlorophthalic anhydride (2·5 g.), aqueous ammonia (25 c.c.; *d* 0·88), and cuprous iodide (0·5 g.) was heated in a sealed tube at 120—130° (8 hours); deep red needles (0·8 g.) separated on cooling and were rapidly filtered off and washed with water; the filtrate soon became black on exposure to air; the needles were freed from an insoluble black impurity by extraction with alcohol (Soxhlet). (b) The foregoing procedure was more satisfactory when 3 : 6-dichlorophthalimide was used instead of the anhydride; the yield was greater (1·2 g.) and there was less amorphous by-product. Modifications of these processes failed to give improvement. 3 : 6-*Diaminophthalimide* formed bright red, acicular needles when separating from alcohol at room temperature but golden-brown plates when crystallised at 100°; the red form slowly changed into the brown when kept. Crystallisation from aniline and nitrobenzene gave the red and the brown form respectively; both forms melted at 298° (decomp.); the brown form appeared more soluble in alcohol (Found: C, 54·35; H, 4·2; N, 23·6. $C_8H_7O_2N_3$ requires C, 54·25; H, 3·95; N, 23·7%). It was readily soluble in glacial acetic acid but sparingly in water; it dissolved without chemical change to a red solution in cold 5% aqueous sodium hydroxide and to a colourless solution in concentrated hydrochloric acid (the hydrochloride formed colourless needles, not hydrolysed in cold water); these solutions were not fluorescent, but the orange or yellow solutions in alcohol, ether, or benzene exhibited green fluorescence. The phthalimide could be diazotised and then coupled with β-naphthol. When boiled (10 mins.) with a mixture of acetic anhydride (4 mols.; 1 vol.) and glacial acetic acid (2 vols.), the phthalimide gave 3 : 6-*diacetamidophthalimide*, in yellow pointed needles (from alcohol) or rhombic plates (from acetic acid), m. p. 321° (decomp.), insoluble in water but soluble to yellow solutions (blue fluorescence) in organic solvents (Found: N, 16·2. $C_{12}H_{11}O_4N_3$ requires N, 16·1%).

3 : 6-*Diamino*-N-*aminophthalimide.*—A mixture of 3 : 6-diaminophthalimide (3·4 g.), hydrazine hydrate (2 g.; 2 mols.), and water (100 c.c.) was refluxed; 3 : 6-*diamino*-N-*aminophthalimide*, which separated during the reaction, crystallised from water (yield, 3·5 g.) in deep scarlet needles of a *monohydrate* (Found: C, 45·7; H, 4·9. $C_8H_8O_2N_4,H_2O$ requires C, 45·7; H, 4·75%), which lost the water at 100° but regained it when exposed to air. The anhydrous substance melted at 282° (Found: C, 49·9; H, 4·3; N, 29·25. $C_8H_8O_2N_4$ requires C, 50·0;

H, 4·2; *N*, 29·15%); *it was moderately readily soluble in water or alcohol and readily soluble* in acetic acid; the orange solutions were only faintly fluorescent (yellow). *It was insoluble in* cold dilute sodium hydroxide, but was partly hydrolysed on boiling.

N-*Amino*-3 : 6-*diacetamidophthalimide*, prepared by heating 3 : 6-diacetamidophthalimide with hydrazine hydrate (1 mol.) in aqueous alcohol (96%), formed long yellow needles, m. p. 304° (decomp.), from water (Found: N, 20·6. $C_{12}H_{12}O_4N_4$ requires N, 20·3%); the benzylidene derivative crystallised in pale yellow needles, m. p. 319° (decomp.). The action of nitrous acid in acetic acid converted it into 3 : 6-diacetamidophthalimide. Both of the above *N*-aminophthalimide derivatives reduced Fehling's solution. 3 : 6-*Diacetamido*-N-*acetamidophthalimide* was prepared, by heating anhydrous 3 : 6-diamino-*N*-aminophthalimide with acetic anhydride (3 mols.), in lemon-yellow prismatic rods (from acetic acid; the solution had a strong light blue fluorescence); it was insoluble in water and melted at 248° (Found: C, 52·3; H, 4·7. $C_{14}H_{14}O_5N_4$ requires C, 52·6; H, 4·7%).

5 : 8-*Diaminophthalaz*-1 : 4-*dione*.—This was prepared in nearly quantitative yield (a) by refluxing 3 : 6-diaminophthalimide with hydrazine hydrate (3 mols.) for 1 hour, the residue being extracted with cold aqueous ammonia (20%), and the filtered extract acidified with acetic acid to precipitate the *dione*; or (b) by similarly treating 3 : 6-diamino-*N*-aminophthalimide with hydrazine hydrate (2 mols.). It formed deep yellow rhombic needles of a *monohydrate* from water (Found: H_2O, 8·4. $C_8H_8O_2N_4,H_2O$ requires H_2O, 8·6%), and was moderately soluble in water or alcohol. Its aqueous solutions, which were acid to litmus and had a very strong green fluorescence, were slowly oxidised in air, rapidly if sodium hydroxide was present. The dione, m. p. 329° (decomp.), was soluble in acetic acid but decomposed on boiling; it did not reduce Fehling's solution (Found, in anhydrous substance: C, 50·1; H, 4·3; N, 29·3. $C_8H_8O_2N_4$ requires C, 50·0; H, 4·2; N, 29·15%). The hydrochloride was hydrolysed by water, but could be diazotised and coupled with β-naphthol. Owing to oxidation, the sodium salt could not be isolated. 5 : 8-*Diacetamidophthalaz*-1 : 4-*dione*, prepared by heating 3 : 6-diacetamidophthalimide or 3 : 6-diacetamido-*N*-acetamidophthalimide with hydrazine hydrate (3 mols.) on a water-bath (½ hour), formed colourless hair-like needles (from water), m. p. 279° (decomp.), and was not fluorescent (Found: C, 52·4; H, 4·5. $C_{12}H_{12}O_4N_4$ requires C, 52·2; H, 4·35%); it dissolved at once in dilute alkalis to colourless solutions, and lost the acetyl groups only on boiling; with acetic anhydride, it was acetylated in the hydrazide ring, giving a *triacetyl* derivative of 5 : 8-diaminophthalaz-1 : 4-dione in small white plates, m. p. 306° (decomp.) (Found: C, 52·5; H, 4·5. $C_{14}H_{14}O_5N_4$ requires C, 52·6; H, 4·7%), which lost the new acetyl group on treatment with alkali in the cold.

3 : 6-*Diacetamidophthalic Anhydride*.—3 : 6-Diamino-*N*-aminophthalimide was warmed on a water-bath with 5% aqueous caustic soda (15 mins.), the resulting solution cooled, and a large excess of concentrated hydrochloric acid added; the hydrochloride of 3 : 6-diaminophthalic acid then crystallised. It was converted, by hydrolysis with a little water, into the acid (white needles, not melted at 340°), and this was dissolved in 5% caustic soda solution and reprecipitated with acetic acid. The crude acid, which still contained a sodium salt, was boiled (10 mins.) with acetic anhydride (4 mols.); the reddish solution crystallised on cooling. 3 : 6-*Diacetamidophthalic anhydride* formed long, pale yellow needles from acetic acid, m. p. 279°; it was insoluble in water but soluble in cold alkalis; its solution in acetic acid had a strong sky-blue fluorescence (Found: C, 54·9; H, 4·05. $C_{12}H_{10}O_5N_2$ requires C, 54·9; H, 3·8%). Hydrazine hydrate (1 mol.) converted it almost completely into *N*-amino-3 : 6-diacetamidophthalimide (m. p. and mixed m. p. 302—304°).

4 : 5-*Dichlorophthalimide* was prepared by heating 4 : 5-dichlorophthalic anhydride (10 g.) with ammonium carbonate (5 g.) at 250° (½ hour). The product was extracted with boiling water, and the residue crystallised from alcohol, the phthalimide separating in colourless rhomboidal plates, m. p. 221° (Found: N, 6·65. $C_8H_3O_2NCl_2$ requires N, 6·45%). Attempts to convert it into 4 : 5-diaminophthalimide by means of ammonia in presence of cuprous iodide led only to a black product insoluble in alcohol.

6 : 7-*Diaminophthalaz*-1 : 4-*dione*.—6 : 7-Dichlorophthalaz-1 : 4-dione (2·5 g.), cuprous iodide (0·5 g.), and aqueous ammonia (50 c.c., *d* 0·88) were heated in a sealed tube at 160—170° (16 hours); the pale yellow solution obtained was filtered and treated with dilute acetic acid; the *dione* (1·8 g.) then separated in small, buff, hexagonal plates, m. p. above 340°; it formed a *dihydrate* from water (Found: C, 42·2; H, 5·3; H_2O, 15·4. $C_8H_8O_2N_4,2H_2O$ requires C, 42·1; H, 5·3; H_2O, 15·8%). The dione, which formed a white sodium salt, was sparingly soluble in water or alcohol and was not fluorescent; it could be diazotised and coupled with phenols; it condensed with phenanthraquinone in glacial acetic acid, giving a *phenanthrazine*

derivative in orange microcrystals, m. p. above 340°, apparently also a dihydrate (Found: C, 66·2; H, 4·1. $C_{22}H_{12}O_2N_4,2H_2O$ requires C, 66·0; H, 4·0%).

Sodium Phthalimide-3-hydrazine-β-sulphonate.—3-Aminophthalimide hydrochloride (2·4 g.), suspended in 16% hydrochloric acid (25 c.c.), was treated with sodium nitrite (1·1 g.) in a little water at 0—5°, and the diazo-solution at once run into an ice-cold solution of sodium sulphite (11 g., heptahydrate) and sodium carbonate (20 g., monohydrate) in water (80 c.c.); after 10 minutes, the orange solution was treated with concentrated hydrochloric acid (30 c.c.) and heated at 100° (½ hour). Crystals separated at 0° overnight, and were recrystallised from boiling water (20 c.c.) and dried at 100° (yield, 2·1 g.). The *sulphonate* formed pale yellow, tetragonal plates, becoming deep yellow when moistened; it reduced Fehling's solution (Found: C, 34·1; H, 2·4; Na, 8·15. $C_8H_6O_5N_3SNa$ requires C, 34·4; H, 2·2; N, 8·25%).

3-*Hydrazinophthalimide*, prepared by warming the above sulphonate and concentrated hydrochloric acid on a water-bath for a few minutes, and treating the resulting white needles of the hydrochloride of 3-hydrazinophthalimide with aqueous ammonia (10%), formed deep yellow needles, m. p. 216° (dried at 100°). Crystallisation from water at 90° converted the substance into a second form, orange-pink rhombic plates, m. p. 208° (Found: in yellow form, C, 54·2; H, 4·2; in orange form, C, 54·1; H, 4·1. $C_8H_7O_2N_3$ requires C, 54·2; H, 4·0%), but rapid crystallisation at a lower temperature gave a mixture of both forms; the mixed m. p. of the two forms was intermediate. Both forms reduced Fehling's solution. They were at once soluble in dilute sodium hydroxide solution, and were precipitated as the yellow form by acetic acid. Crystallisation from cold water gave a mixture of both forms, but with benzene there was no interconversion. The substance is not fluorescent.

N-*Amino-3-hydrazinophthalimide*.—3-Hydrazinophthalimide (1·7 g.), hydrazine hydrate (0·5 g.; 1 mol.), and alcohol (50 c.c.; 96%) were boiled under reflux (2 hours); the crystals which remained were washed with dilute sodium hydroxide solution to remove a little unchanged hydrazinophthalimide. N-*Amino-3-hydrazinophthalimide* formed orange-red prisms (from alcohol), m. p. 202°, only slightly soluble in water (Found: C, 50·2; H, 4·3. $C_8H_8O_2N_4$ requires C, 50·0; H, 4·15%), which reduced Fehling's solution.

Sodium N-*Aminophthalimide-3-hydrazine-β-sulphonate*.—A mixture of sodium phthalimide-3-hydrazine-β-sulphonate and hydrazine hydrate (1 mol. or 3 mols.) in alcohol (96%) was heated under reflux (2 hours); ammonia was evolved and the yellow plates of the initial salt were gradually replaced by pale orange rods of the desired *compound*. This was sparingly soluble in alcohol, from which it separated unchanged (Found: C, 32·8; H, 2·7; Na, 7·8. $C_8H_7O_5N_4SNa$ requires C, 32·7; H, 2·4; Na, 7·8%); it was very soluble in hot water, in which it changed rapidly into the following salt, which separated in white hairy needles.

Sodium Phthalaz-1 : 4-*dione-5-hydrazine-β-sulphonate*.—Sodium phthalimide-3-hydrazine-β-sulphonate (1·2 g.), hydrazine hydrate (1 mol. or 3 mols.), and water (10 c.c.) were heated at 100° (½ hour), ammonia being evolved. Acidification of the solution with dilute acetic acid precipitated the dione *salt* in white hairy needles, readily soluble in water (Found: C, 32·6; H, 2·6; Na, 7·9. $C_8H_7O_5N_4SNa$ requires C, 32·7; H, 2·4; Na, 7·8%). Warm hydrochloric acid converted it into 5-hydrazinophthalaz-1 : 4-dione (below).

5-*Hydrazinophthalaz*-1 : 4-*dione*.—(a) 3-Hydrazinophthalimide or N-amino-3-hydrazinophthalimide was heated with an excess of hydrazine hydrate and water; (b) sodium phthalaz-1 : 4-dione-5-hydrazinesulphonate was warmed with concentrated hydrochloric acid. A solution of the resulting colourless needles of the hydrochloride of the required dione in warm aqueous caustic soda (2%) was acidified with acetic acid; the *dione* separated in white rhombic platelets, m. p. 312° (decomp.), which reduced Fehling's solution (Found: C, 49·9; H, 4·3. $C_8H_8O_2N_4$ requires C, 50·0; H, 4·15). It was non-fluorescent, and darkened slowly when kept, as did also its colourless *sodium* salt (Found: Na, 10·45. $C_8H_7O_2N_4Na$ requires Na, 10·75%), but its hydrochloride was stable.

Pyromellitaz-1 : 4 : 6 : 9-*tetraone*.—Pyromellitic acid, m. p. 265°, was converted into its dianhydride by boiling with acetic anhydride. The dianhydride (1·2 g.), dissolved in hot glacial acetic acid (50 c.c.), was mixed with hydrazine hydrate (0·6 g.) in acetic acid (10 c.c.) and boiled under reflux (1 hour); the yellow plates which separated initially were converted into a buff powder (1·26 g.). This was dissolved in hot dilute sodium hydroxide solution; acidification with acetic acid precipitated the *tetraone* as a white powder, insoluble in all ordinary solvents and devoid of reducing properties (Found: C, 48·5; H, 2·7; N, 23·0. $C_{10}H_6O_4N_4$ requires C, 48·8; H, 2·4; N, 22·8%). Its *sodium* salt, sulphur-yellow rods, readily soluble in hot water, appeared to be a tetrahydrate of the disodium compound, but there was no loss of water at 150° (Found: Na, 12·6, 12·9. $C_{10}H_4O_4N_4Na_2,4H_2O$ requires Na, 12·7%).

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(*Addendum, April 9th*) Rowe and Peters have repeated the preparation of the acetyl derivatives of phthalaz-1 : 4-dione (this vol., p. 25) and are in agreement with the constitutions (p. 19) attributed to the diacetyl and the two monoacetyl derivatives (private communication).

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133. *Modified Cinchona Alkaloids. Part IV. Constitution.*

By Thomas A. Henry, William Solomon, and Egbert M. Gibbs.

The substances described in this and Parts I and II (J., 1934, 1923; 1935, 966; Part III, Goodson, J., 1935, 1094) as produced by the action of boiling 60% sulphuric acid on quinine and quinidine are of three kinds: (1) isomerides of the two alkaloids, (2) demethylated (phenolic) bases corresponding to these isomerides, and (3) hydration products of (1) and (2). Sufficient information has now been obtained to warrant discussion of the formulæ to be assigned to these substances. The authors have confined their attention to the products formed by the action of sulphuric acid, but similar products are obtained when the cinchona alkaloids are treated with other mineral acids, as well as by the dehalogenation, by alkalis or silver salts, of the halogeno-dihydro-bases formed by the addition of a molecule of one of the halogen acids, usually hydrogen bromide or iodide, to the vinyl side chain of any one of the normal cinchona alkaloids.

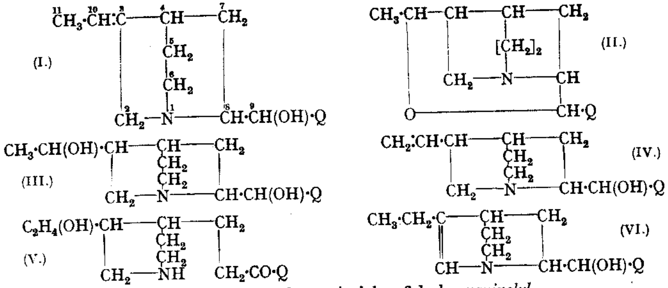
It is possible to account for the reactions of many of these substances on the basis of formulæ (I) to (III), which are accepted for certain transformation products of cinchonidine and cinchonine. A detailed account of the investigations which resulted in the development of these formulæ has been published by Jungfleisch and Léger (*Ann. Chim.*, 1920, **14**, 59).

An inspection of these formulæ will show that substances of type (I) should exist in two geometrically isomeric forms; those of type (II), which are found only in the dextrorotatory series, in two epimeric forms about the new centre of asymmetry at carbon atom 10; and those of type (III) in two stereoisomeric forms. Most of these forms are now known for the four alkaloids under consideration, but only one form of type (I) and one of type (III) are known for cinchonine and cinchonidine respectively. Quinidine yields a third isomeride of type (II) and an isomeride of a new type; these two unexpected forms are discussed later.

The experimental portion of the paper is concerned mainly with (1) the methods by which assignment of each transformation product of quinine and quinidine to its particular type has been made, (2) an investigation of the nature of the side chain in each of the three types, and (3) descriptions of certain of the transformation products now isolated for the first time. In discussing these substances the notation suggested by Rabe and Riza (*Annalen*, 1932, **496**, 152) with the addition of the numbers 10 and 11 for the two-carbon side chain, as shown in formula (I), has been used. The principal data required for the classification of the transformation products have been assembled in a table (p. 593) in which the name of each *apo*- or phenolic base is placed under the name of the methyl ether to which it is related when this is known. For the sake of simplicity these *apo*- or phenolic bases are ignored in the following discussion, except where they exhibit some peculiarity.

In obtaining these data the authors have used methods differing from those employed by their predecessors. Acylation of cinchona alkaloids is unsatisfactory, as the products are often amorphous, and Zerewitinoff determinations of replaceable hydrogen (RH), which in these cases can only mean hydrogen in hydroxyl groups, have been used instead. No difficulty was experienced in deciding by this means between type (I) (RH = 1), type (II) (RH = 0) and type (III) (RH = 2) so far as this factor is concerned. With the *apo*-

or phenolic bases, which are insoluble in the ethereal solvents usually used in this process, pyridine had to be used as a solvent and as this, even after rigorous drying, gave an



Q = *quinolyl*, 6-*methoxyquinolyl* or 6-*hydroxyquinolyl*.

undesirably large yield of methane in blank experiments, an unusually large quantity (0·5 to 1·0 g.) of the phenolic base had to be used to get trustworthy results.

Name of alkaloid.	Hydroxyl, % (Zerewitinoff). Found.	Calc.	*C*-Me, % (Kuhn–Roth). Found.	Calc.	$[\alpha]_D^{16°}$.	Structural type.
Quinine	6·3	1 = 5·2	nil	nil	− 284·5°	IV
Cupreine	—	—	—	—	− 283·5	,,
α-*iso*Quinine	5·15	1 = 5·2	7·7	1 = 8·3	− 364·3	I
*isoapo*Quinine	10·5	2 = 10·9	—	—	− 356·7	,,
β-*iso*Quinine	6·0	1 = 5·2	8·6	1 = 8·3	− 295·9	,,
*apo*Quinine	11·1	2 = 10·9	—	—	− 281·0	,,
α-Hydroxydihydroquinine	9·3	2 = 9·9	5·2	1 = 7·9	− 197·5	III
α-Hydroxydihydro*apo*quinine	14·9	3 = 15·5	—	—	− 205·4	,,
β-Hydroxydihydro*apo*quinine [a]	14·0	3 = 15·5	9·4	1 = 8·2	− 205·1	,,
Quinidine [b]	6·2	1 = 5·2	nil	nil	+ 334·2	IV
*apo*Quinidine methyl ether	5·0	1 = 5·2	7·9	1 = 8·3	+ 277·6	I
*apo*Quinidine	10·7	2 = 10·9	—	—	+ 291·4	,,
*neoiso*Quinidine	5·5	1 = 5·2	8·0	1 = 8·3	+ 197·2	,,
*neoapo*Quinidine	10·7	2 = 10·9	—	—	+ 206·2	,,
ψ-Quinidine [b]	5·3	1 = 5·2	6·5	1 = 8·3	+ 249·2	VI
α-*iso*Quinidine [b]	nil	nil	6·9	1 = 8·3	+ 125·2	II
β-*iso*Quinidine	nil	nil	6·0	1 = 8·3	+ 29·0	,,
*isoapo*Quinidine	5·9	1 = 5·5	—	—	+ 25·0	,,
γ-*iso*Quinidine [b]	nil	nil	6·3	1 = 8·3	+ 67·8	,,
α-Hydroxydihydroquinidine	—	—	—	—	+ 241·5	III
α-Hydroxydihydro*apo*quinidine	14·7	3 = 15·5	—	—	+ 252·6	,,
Hydroxydihydroquinidine	9·5	2 = 9·9	4·9	1 = 7·9	+ 225·3 [c]	,,
β-Hydroxydihydro*apo*quinidine	17·1	4 [d] = 18·2	—	—	+ 224·6 [c]	,,

[a] Corresponding methyl ether unknown.
[b] Corresponding phenolic base unknown.
[c] In alcohol. [d] One hydroxyl due to retained alcohol.

Catalytic hydrogenation of substances of type (I) should add on one molecule of hydrogen at C_3–C_{10}, producing, *e.g.*, dihydroquinine from α- and β-*iso*quinines and dihydroquinidine from the two quinidine isomerides of this type. In this process carbon atom 3 becomes a centre of asymmetry, as it is in the normal cinchona alkaloids (IV), so that the dihydro-base formed should be a mixture of two epimerides about carbon atom 3. This proved to be the case. Thus α- and β-*iso*quinine yielded dihydroquinine and *epi*-C_3-dihydroquinine, while *apo*quinidine methyl ether gave dihydroquinidine and *epi*-C_3-dihydroquinidine. Both *neoiso*quinidine and ψ-quinidine similarly yielded dihydroquinidine, but the C_3-epimeride has not been isolated in a pure state in these cases.

In the hydrogenation of the quinine and quinidine isomerides of type (I), it is the dihydro-

base of higher rotation which is formed in predominant quantity, *viz.*, the C_3-epimeride from the quinine isomerides and dihydroquinidine from those of quinidine.

This is the first instance in which substances are described which are stereoisomeric with the natural cinchona alkaloids and differ from them only in respect of the relative configuration of C_3 to C_4. Rabe *et al.* (*Annalen*, 1932, **492**, 242) have obtained the C_8- and C_9-epimerides, such as "*epi*hydroquinine" and "*epi*hydroquinidine," in which the configuration at C_3 and C_4 is identical with that of the parent alkaloids, and have synthesised the complete enantiomorphs, *d*-dihydroquinine and *l*-dihydroquinidine (Rabe and Schultze, *Ber.*, 1933, **66**, 120), in which C_3 and C_4 taken together have the opposite configuration. The present results, therefore, showing as they do that in dihydroquinine and dihydroquinidine, as probably also in the other natural cinchona alkaloids, carbon atom 3 must be dextrorotatory, constitute the first evidence of the configuration at one of these atoms taken by itself.

The nature of the side chain in the transformation products of all three types has been investigated by Kuhn's method for the estimation of methyl groups attached to carbon (Kuhn and Roth, *Ber.*, 1933, **66**, 1274; Kuhn and L'Orsa, *Z. angew. Chem.*, 1931, **44**, 847). With one exception each of the quinine and quinidine isomerides of type (I) gave results clearly indicating the presence of one such group, and supporting the representation of the side chain in type (I) as $\vdots CH{\cdot}CH_3$. Confirmation of this result was attempted by an ozonisation experiment in which it was expected that acetaldehyde would be produced. The result was disappointing, only a small yield of the aldehyde being obtained. ψ-Quinidine, the unexpected third isomeride of quinidine, gave a low result in the Kuhn–Roth estimation. Since it also produces a mixture of dihydroquinidine and *epi*-C_3-dihydroquinidine on catalytic hydrogenation, C_3 must be the centre of asymmetry produced in the hydrogenation, and it is suggested that this third isomeride should be represented by formula (VI), with the ethylenic linkage between C_3 and C_2, the side chain becoming $CH_3{\cdot}CH_2$. This accounts for the one replaceable hydrogen found, the formation of two epimeric dihydroquinidines on hydrogenation, and for the low result of the Kuhn–Roth *C*-Me estimation, as it has been found that dihydroquinine and dihydroquinidine, where the side chain is also $\cdot CH_2{\cdot}CH_3$, give by the Kuhn–Roth method values for *C*-Me of about the same order.

Formula (II) has been generally accepted as representing the stereoisomeric α- and β-*iso*cinchonines. In investigating the validity of this formula for α-*iso*cinchonine, Rabe and Böttcher (*Ber.*, 1917, **50**, 128) showed that this substance undergoes the normal Pasteur conversion into hydroxydihydrocinchonicine (V), but were unable to decide between the structures (i) $R{<}^{CH\cdot CH_3}_{O}$ and (ii) $R{<}^{CH_2}_{O}{>}CH_2$ for the side chain C_{10}—C_{11}. The three substances of type (II) now dealt with, α-, β-, and γ-*iso*quinidines, showed all the characteristics of the type: relative stability to potassium permanganate, absence of replaceable hydrogen, and failure to hydrogenate. In the Kuhn–Roth estimations the three isomerides gave results, which, though unexpectedly low, favour the side chain (i) rather than (ii).

Domański and Suszko (*Rec. trav. chim.*, 1935, **54**, 481), who first obtained γ-*iso*quinidine, point out its great similarity to α-*iso*quinidine (*Bull. Inter. Acad. Polonaise*, 1933, *A*, 119) and suggest that these are epimerides about carbon atom 3, both belonging to type (II), to which Konopnicki and Suszko (*ibid.*, 1929, *A*, 340) were the first to assign β-*iso*quinidine. In making this suggestion, the Polish authors recognise the difficulties of such an assumption as pointed out in another connection by Rabe *et al.* (*Annalen*, 1932, **492**, 251). In the present authors' view the information available is insufficient to decide the question, but in this connection the following table is interesting.

		Assumed direction of asymmetry.	
	$[\alpha]_D^{15°}$.	Carbon atom 10.	Carbon atom 9.
β-*iso*Quinidine	+ 29·0°	−	−
γ-*iso*Quinidine	+ 67·8	+	−
α-*iso*Quinidine	+ 125·2	−	+

There is evidence that carbon atom 9 makes the largest contribution to the total value specific rotation of any one alkaloid in this group : thus epimerisation about this

centre changes the specific rotation of quinidine, + 243·5°, to that of *epi*quinidine, + 102·4° (Rabe *et al.*, *ibid.*, p. 252). The small dextro-contribution made by carbon atoms 3 and 4 to the total dextrorotation of quinidine is evidenced by the fall in rotation, + 243·5° (alcohol) to + 38° (chloroform), when quinidine is converted into quinicine, in which asymmetry at carbon atoms 8 and 9 disappears. It seems possible, therefore, that the large changes in rotation produced by the conversion of quinidine into α-, γ-, and β-*iso*quinidines are due in the first place to lævorotation at carbon atom 10, in the second to lævorotation at carbon atom 9, and in the third to both these changes. It is not unreasonable to suppose that epimerisation can occur at C_9 under the conditions of these experiments, since Rabe, Haeuszler, and Hochstätter (*Annalen*, 1934, **514**, 63) have shown that Emde's supposed "hydrocinchonicine," produced by the action of 25% hydrochloric acid on dihydrocinchonidine (*Helv. Chim. Acta*, **1932**, **15**, 557), is in reality *epi*dihydrocinchonidine (*epi*-C_9-dihydrocinchonidine) and Fiedzuiszko and Suszko found that dihydrocinchonine can be epimerised about C_9 in the same manner (*Bull. Inter. Acad. Polonaise*, **1934**, *A*, 415). Further, there is at present no evidence that in all these isomerides of type (II) the ether-oxide linkage is between carbon atoms 9 and 10. It is possible that in one of them it is at C_3—C_9.

Although somewhat unsatisfactory, the results of the Kuhn–Roth estimation of :CMe· groups for the hydration products (type III) clearly indicate that in these substances the side chain is of the form CH_3·CH·OH.

It has not been possible in all cases to obtain both the phenolic bases and their methyl ethers, because *O*-methylation of the former gives small yields and demethylation of the latter usually leads to mixtures, so that considerable quantities of material are necessary for the establishment of such relationships. It has, however, been possible to relate the phenolic base to its methyl ether in most cases, and in this connection it is of interest to mention that α-*iso*quinine, discovered by Böttcher and Horowitz a quarter of a century ago (*Monatsh.*, 1911, **32**, 793), is now shown to be the methyl ether of *isoapo*quinine (Part II, p. 967).

"allo*Quinidine*."—While this paper was in preparation Ludwiczac and Suszko published (*Bull. Inter. Acad. Polonaise*, 1936, *A*, 276) a description of a supposed new isomeride of quinidine, produced by the action of 70% sulphuric acid on quinidine at 60—70° for 100 hours. This product is named *allo*quinidine and is stated to have m. p. 249—250° and $[\alpha]_D$ + 230° (*c* = 1, alcohol). A specimen of this material has been prepared by the present authors by the prescribed process. It had m. p. 248—250°, $[\alpha]_D$ + 219·3° (*c* = 1, alcohol), but on recrystallisation from alcohol the m. p. gradually rose to 256—257° and the specific rotation to + 224·6° (*c* = 1, alcohol), which are the constants of hydroxydihydroquinidine (p. 598), and a mixture with that substance showed no depression of melting point. *allo*-Quinidine appears therefore to be merely impure hydroxydihydroquinidine, and the Polish authors' description of the base, as appreciably soluble in water, and giving low carbon results for $C_{20}H_{24}O_2N_2$ on combustion, is in harmony with that view.

Experimental.

In the following account the combustion results are in all cases from micro-analyses. Unless stated otherwise, the specific rotations are for $c = M/40$ for the dry substance: the solvent is *N*/10-sulphuric acid for bases, and water for salts.

Quinidine Transformation Products. Type (I).

Two substances of this group have been described already, *viz.*, *apo*quinidine and its methyl ether (Part II, pp. 969, 971). Two more are now dealt with, *viz.*, neoapo*quinidine* and its methyl ether, neoiso*quinidine*.

ψ-Quinidine (type VI) is dealt with at the end of this group, from which it differs only in the position of the ethylenic linkage. The *apo*-base corresponding to ψ-quinidine has not been obtained.

neoapo*Quinidine* (type I; Q = 6-hydroxyquinolyl).—A preliminary description of this substance was given in Part II (p. 970) under the name "phenolic base A." It is best isolated as the hydrochloride from the mother-liquors obtained in the purification of *apo*quinidine (Part II, p. 969), and is then recrystallised, first from water and finally from alcohol (96%).

From this salt the base is recovered as usual. The yield is about 4% of the crude "*apo*quinidine" obtained, which is equivalent to 3% of the quinidine used. neoapo*Quinidine* crystallises from ether or alcohol in needles, m. p. 260°, $[\alpha]_D^{15°} + 206.2°$ or $+ 120.7°$ ($c = 1$, alcohol) (Found: C, 73·5; H, 6·9; N, 8·8. $C_{19}H_{22}O_2N_2$ requires C, 73·5; H, 7·2; N, 9·0%). The *hydrochloride* crystallises from alcohol (96%) in hexagonal prisms or from water in rectangular prisms. Both forms have m. p. 197° and $[\alpha]_D^{15°} + 110.4°$ (Found: loss at 120° in a vacuum, 4·7. $C_{19}H_{22}O_2N_2,HCl,H_2O$ requires H_2O, 4·9%. Found for dry salt: N, 7·5; C, 10·3. $C_{19}H_{22}O_2N_2$,HCl requires N, 8·1; Cl, 10·2%). The *dihydrochloride* separates from water in small rectangular prisms, m. p. 255° (decomp.) with some sintering at 190°, $[\alpha]_D^{15°} + 167.0°$ (Found: loss on drying at 120° in a vacuum, 9·9%. Found for dry salt: N, 7·2; Cl, 17·3. $C_{19}H_{22}O_2N_2$,2HCl requires N, 7·3; Cl, 18·5%). Combustion results for carbon in these two salts were persistently low: figures for chlorine were also low for the dihydrochloride, probably owing to dissociation on recrystallisation from water, as has been noticed in other cases in this series (Part I, p. 1928; Part II, p. 967). The *nitrate* crystallises from dry alcohol in colourless prisms, becomes yellow on exposure to light, has m. p. 100° (air-dry, decomp.), but after drying begins to discolour at 135° and is completely decomposed at 160°; $[\alpha]_D^{15°} + 102.2°$ (Found: loss on drying first at 90° and finally at 115° in a vacuum, 18·6%. Found for dry salt: C, 61·2; H, 6·1; N, 11·1. $C_{19}H_{22}O_2N_2,HNO_3$ requires C, 61·1; H, 6·2; N, 11·3%). The *neutral sulphate* crystallises from alcohol in bright yellow leaflets, m. p. 80° or 218—220° (dry, decomp.) [Found for salt dried in a vacuum first at 60°, then at 120°: C, 61·8; H, 6·0; N, 7·1; S, 4·9. $(C_{19}H_{22}O_2N_2)_2,H_2SO_4,H_2O$ requires C, 61·9; H, 6·5; N, 7·6; S, 4·4%].

With diazomethane *neoapo*quinidine gave an 80% yield of the methyl ether, m. p. 83—84°, $[\alpha]_D^{15°} + 197.2°$ (Found: loss on drying in a vacuum at 45°, 10·4. Calc. for $C_{20}H_{24}O_2N_2,2H_2O$: loss, 10·0%), identical with *neoiso*quinidine described in the next paragraph.

neoiso*Quinidine* (Type I; Q = 6-methoxyquinolyl).—This isomeride of quinidine was referred to in a preliminary manner in Part II (p. 971). The crude material then obtained has now been found to be a mixture of two substances, neoiso*quinidine* and *ψ-quinidine*, which were separated by crystallisation of the neutral sulphates from dry alcohol (1 g. in 2 c.c.), and of the final residues from water (1 g. in 1 c.c.), the separation being controlled polarimetrically. *neoiso*-Quinidine crystallises from ether in long prisms, m. p. 83°, $[\alpha]_D^{15°} + 198.6°$ or $+ 98.7°$ ($c = 1$, alcohol) (Found: loss on drying at 45° in a vacuum, 10·1. $C_{20}H_{24}O_2N_2,2H_2O$ requires H_2O, 10·0%. Found in dry base: C, 74·0; H, 7·4; N, 8·6; MeO, 9·3. $C_{20}H_{24}O_2N_2$ requires C, 74·0; H, 7·5; N, 8·6; MeO, 9·6%). A mixed m. p. determination with *neoapo*quinidine methyl ether (previous paragraph) showed no depression. The *nitrate* separates from water in prisms. The air-dry substance has m. p. 115° and re-melts at 218°; the dry substance has m. p. 220° (decomp.), $[\alpha]_D^{15°} + 100.6°$ (Found: loss on drying at 120° in a vacuum, 4·8. $C_{20}H_{24}O_2N_2,HNO_3,H_2O$ requires loss, 4·4%. Found for dry salt: C, 62·5; H, 6·3; N, 10·9; MeO, 7·8. $C_{20}H_{24}O_2N_2,HNO_3$ requires C, 62·0; H, 6·5; N, 10·85; MeO, 8·0%).

ψ-Quinidine (Type VI; Q = 6-methoxyquinolyl).—This substance occurs with *neoiso*-quinidine as described above, and is separated by taking advantage of the lower solubility in dry alcohol of its neutral sulphate. For final purification the latter is converted into the nitrate, and this recrystallised from boiling alcohol (1 g. in 4 c.c.). The *base* recovered from the pure nitrate crystallises from boiling alcohol (1 g. in 3 c.c.) in colourless prisms, m. p. 85—90° (air-dry) or 150—155° (dried at 80—115° in a vacuum), $[\alpha]_D^{15°} + 249.4°$ (Found: loss in a vacuum, first at 80° and finally at 115°, 12·0. $C_{20}H_{24}O_2N_2,C_2H_5\cdot OH$ requires loss, 12·4%. Found for dry substance: C, 74·2; H, 7·7; N, 8·4; MeO, 9·2. $C_{20}H_{24}O_2N_2$ requires C, 74·0; H, 7·5; N, 8·6; MeO, 9·6%). The *hydrochloride* crystallises from water in anhydrous prisms, m. p. 269° (decomp.) (Found: C, 66·6; H, 7·1; N, 7·8; Cl, 9·9; MeO, 8·5. $C_{20}H_{24}O_2N_2$,HCl requires C, 66·6; H, 6·9; N, 7·8; Cl, 10·0; MeO, 8·6%). The *nitrate* separates from boiling alcohol in anhydrous rhombic prisms, m. p. 217—218° (decomp.) (Found: C, 62·5; H, 6·6; N, 10·5; MeO, 7·8. $C_{20}H_{24}O_2N_2,HNO_3$ requires C, 62·0; H, 6·5; N, 10·85; MeO, 8·0%).

Hydrogenation of Quinidine Isomerides (Types I and VI).—Preliminary experiments showed that *apo*quinidine hydrochloride and *neoapo*quinidine dihydrochloride could be hydrogenated in $N/10$-sulphuric acid solution in the presence of Adams's platinic oxide as catalyst. The reduced product was in each case converted into the neutral hydrochloride, which after a single crystallisation from water had in the two cases m. p. 238—240°, $[\alpha]_D^{15°} + 188.9°$ and m. p. 239—240°, $[\alpha]_D^{15°} + 180.4°$. These figures approximate to those of dihydrocupreidine hydrochloride, m. p. 231—233°, $[\alpha]_D^{15°} + 194°$, but, as the dihydrocupreidines proved less easy to separate than their methyl ethers, recourse was had to hydrogenation of the methyl ethers of these *apo*-bases.

Hydrogenated under these conditions, *apo*quinidine methyl ether absorbed about 1% more than the calculated amount of hydrogen. The product, isolated in the usual manner, and crystallised once from alcohol, had m. p. 167° and $[\alpha]_D^{15°}$ + 286·9°. After three further crystallisations (1 g. in 5 c.c.) the m. p. was 171—172° and $[\alpha]_D^{15°}$ + 298·3°. The product then showed no depression of m. p. on admixture with dihydroquinidine, m. p. 171—172°, $[\alpha]_D^{15°}$ + 299·0°. The mother-liquors gave more dihydroquinidine on concentration, the total yield being 63% of the crude product. From the final mother-liquors there was obtained in small yield by crystallisation from ether a substance, m. p. 112° (air-dry) or 151—152° (dry), $[\alpha]_D^{15°}$ + 233·8° (Found: loss on drying at 120° in a vacuum, 7·0%. Found for dry base: C, 73·8; H, 8·2; N, 8·4; MeO, 9·6. $C_{19}H_{26}O_2N_2$ requires C, 73·6; H, 8·0; N, 8·6; MeO, 9·5%). This, as already stated, must be epi-C_3-*dihydroquinidine.*

*neoiso*Quinidine (0·6 g.), reduced under similar conditions, furnished an initial product, which after one crystallisation from alcohol had m. p. 168°, $[\alpha]_D^{15°}$ + 290·4°, and yielded after two further crystallisations, dihydroquinidine, m. p. 171—172°, $[\alpha]_D^{15°}$ + 297·5°. ψ-Quinidine (0·53 g.) similarly yielded a crude product, m. p. 170°, $[\alpha]_D^{15°}$ + 292·0, from which dihydroquinidine, m. p. and mixed m. p. 171—172°, $[\alpha]_D$ + 296·6°, was obtained, but in this case and that of *neoiso*quinidine (see above) the C_3-epimeride was too small in amount to be isolated from the residual mother-liquors.

Quinidine Transformation Products. Type (II).

Of the three quinidine isomerides of this group, β-*iso*quinidine has been described already (Part II, p. 970) and its position established as the methyl ether of *isoapo*quinidine (Part I, p. 1929). These results have been confirmed by Ludwiczak and Suszko (*Bull. Inter. Acad. Polonaise*, 1935, *A*, 65), who, however, re-named the phenolic base β-*iso*cupreidine.

Under the conditions used by the present authors, *viz.*, boiling quinidine with 60% sulphuric acid, α- and γ-*iso*quinidines are not found in the reaction mixture, but according to Domański and Suszko (*ibid.*, p. 465), when quinidine is digested with 70% sulphuric acid (*d* 1·615) at 60—70° during 20 hours, β- and γ-*iso*quinidines are produced. On repeating this experiment, the present authors were able to isolate all three isomerides together with some hydroxydihydroquinidine. With 50% sulphuric acid (*d* 1·40) at 65—70° for 20 hours, the whole of the quinidine was recovered unchanged. At 100° for the same period and the same strength of acid, about 40% of the quinidine can be recovered and the reaction products are, as with 70% acid at 60—70°, α-, β- and γ-*iso*quinidines with hydroxydihydroquinidine.

It appears that, as Domański and Suszko found, α- and γ-*iso*quinidines are less stable to sulphuric acid than β-*iso*quinidine and that the survivals in this reaction depend more on the temperature than upon the strength of the acid used.

The Polish authors (*loc. cit.*; *Rec. trav. chim.*, 1935, **54**, 481) have also prepared α- and γ-*iso*quinidines by dehalogenating the crude hydrogen chloride or hydrogen bromide addition products of quinidine with potassium hydroxide in alcohol. The following method of isolating and separating the two isomerides is shorter and gives better yields than that described by them. The largely amorphous hydriodide precipitate, prepared from the crude mixture of bases, is dissolved in alcohol (1 g. in 1 c.c.) and left to deposit quinidine hydriodide. The mixed bases are recovered from the alcoholic mother-liquor and converted into cuprichlorides (1 g. of base, 1 g. of cupric chloride, 5 c.c. of concentrated hydrochloric acid), from which the bases are recovered in the usual way (Buttle, Henry, and Trevan, *Biochem. J.*, 1934, **28**, 435), dried in a vacuum, and dissolved in diluted acetone (1 g. in 1 c.c. + 0·5 c.c. of water). From this solution, nearly pure α-*iso*quinidine crystallises (yield, 57% of the quinidine used). The residue left on removal of the solvent from the mother-liquors, on solution in cold 10% nitric acid, gives γ-*iso*quinidine acid nitrate, of which a further quantity is obtained by dissolving the bases recovered from the cuprichloride mother-liquors in 10% nitric acid (yield, 15%). Additional quantities can be recovered by repeating the process with the residual bases, which also yield a little of Suszko's niquidine and about 3% of *apo*quinidine methyl ether.

α-iso*Quinidine.*—The base is purified by crystallisation from boiling acetone (1 g. in 2 c.c.) twice, from which it separates in anhydrous prisms, m. p. 136—137°, or from 66% aqueous acetone in rhombohedra containing $2H_2O$, m. p. 77°, $[\alpha]_D^{15°}$ + 125·2° or + 109·0° (c = 1, alcohol) (Found: loss on drying at 45° in a vacuum, 10·1; calc. for $2H_2O$, 10·0%. Found for dry substance: C, 74·2; H, 7·4; N, 8·4; MeO, 9·1. Calc. for $C_{20}H_{24}O_2N_2$: C, 74·0; H, 7·5; N, 8·6; MeO, 9·6%). Domański and Suszko give for the product crystallised from aqueous acetone and containing $1H_2O$, m. p. 80° or 130—133° from dry acetone, and $[\alpha]_D^{15°}$ + 111° (c = 0·7815, 96% alcohol). The hydrochloride, $B,HCl,4H_2O$, had m. p. 88—90° or 237° (dry)

and $[\alpha]_D^{15°}$ + 20·3°; Domański and Suszko give m. p. 224°, $[\alpha]_D^{15°}$ + 16° (*c* = 0·8, water). α-*iso*Quinidine could not be hydrogenated in presence of Adams's platinic oxide catalyst.

γ-isoQuinidine acid nitrate, isolated as described, was purified by recrystallisation from boiling water (1 g. in 8 c.c.); the base recovered from it crystallised from wet ether in long prisms, m. p. 83—84° (air-dry), $[\alpha]_D^{15°}$ + 67·8° or + 51° (alcohol) (Found: loss on drying at 120° in a vacuum, 10·25. Calc. for $C_{20}H_{24}O_2N_2,2H_2O$: loss, 10·0%. Found for dry substance: C, 74·3; H, 7·45; N, 8·7; MeO, 9·6. Calc. for $C_{20}H_{24}O_2N_2$: C, 74·0; H, 7·5; N, 8·6; MeO, 9·6%). The neutral hydrochloride has m. p. 163—165°, $[\alpha]_D^{15°}$ − 12·6° (water) (Found: loss on drying at 120° in a vacuum, 6·3. Calc. for $C_{20}H_{24}O_2N_2,HCl,1{\cdot}5H_2O$: loss, 6·9%). The dinitrate crystallises from boiling water in anhydrous needles, m. p. 213° (decomp.), $[\alpha]_D^{15°}$ + 53·3° (water). Domański and Suszko (*loc. cit.*) give for γ-*iso*quinidine, needles, m. p. 70°, $[\alpha]_D^{16°}$ + 51·1° (*c* = 0·9, alcohol); dinitrate, needles, m. p. 196°, $[\alpha]_D^{16°}$ + 50° (water). γ-*iso*Quinidine, like the α-and β-isomerides, resisted catalytic hydrogenation.

Quinidine Transformation Products. Type (III).

The products so far obtained are α-hydroxydihydro*apo*quinidine and its methyl ether, and β-hydroxydihydro*apo*quinidine, with what is possibly its methyl ether, though the two have not yet been definitely related.

*α-Hydroxydihydro*apo*quinidine* (III; Q = 6-hydroxyquinolyl).—This substance is best prepared from the ethereal extract of the carbonated precipitation liquors as described for the analogous derivative of quinine (Part II, p. 968). The extract amounts to about 4% by weight of the quinidine used. On solution in alcohol (1 g. in 1 c.c.) and neutralisation by dilute hydrochloric acid (10%), it yielded a crop of neutral hydrochloride, which was purified by crystallisation from alcohol, water, and 40% alcohol in succession. The *base* was recovered by pouring a solution of the salt in dilute hydrochloric acid into excess of sodium hydroxide solution, passing carbon dioxide into the liquid, and subjecting the latter to prolonged automatic extraction with ether. It crystallises from ether in prisms, which after drying in a vacuum, first at 60° and finally at 120°, swell at 170° and melt to a clear liquid at 205°, $[\alpha]_D^{15°}$ + 252·6° or + 204·7° (*c* = 1, alcohol) (Found: loss on drying at 120° in a vacuum, 11·1%. Found for dry substance: C, 69·7; H, 7·6; N, 8·1. $C_{19}H_{24}O_3N_2$ requires C, 69·5; H, 7·4; N, 8·5). The *hydrochloride* forms small needles, m. p. 203—204°, $[\alpha]_D^{15°}$ + 165·3° (Found: loss on drying at 120° in a vacuum, 4·9. $C_{19}H_{24}O_3N_2,HCl,H_2O$ requires H_2O, 4·7%. Found for dry salt: N, 7·3; Cl, 9·5. $C_{19}H_{24}O_3N_2,HCl$ requires N, 7·7; Cl, 9·7%). With diazomethane the base gave a poor yield (30%) of methyl ether, crystallising from acetone, or alcohol–ether, in prisms, m. p. 145—150°, $[\alpha]_D^{15°}$ + 241·5° (Found: loss on drying at 120° in a vacuum, 4·9%). This methyl ether has not been found among the quinidine transformation products.

*β-Hydroxydihydro*apo*quinidine* (III; Q = 6-hydroxyquinolyl).—The mother-liquors from the separation of the neutral hydrochloride of the α-hydroxy-base are rendered just acid to Congo-red paper with hydrochloric acid and evaporated to dryness, and the residue of acid hydrochloride dissolved in the minimum quantity of boiling absolute alcohol. The crop is a mixture of acid hydrochlorides of the two hydroxy-bases. It is reconverted into neutral hydrochloride, and recrystallised once from alcohol, and then from water (1 g. in 4 c.c.) until the specific rotation is constant. The *base* crystallises from alcohol in small prisms, m. p. 190° (decomp.), $[\alpha]_D^{20°}$ + 197° (*c* = 0·5, alcohol), which is equivalent to + 224·6° for the base free from the retained molecule of alcohol. It loses nothing on drying at 115° in a vacuum, but the analytical results indicate that it still retains one mol. of alcohol (Found: C, 67·3; H, 8·4; N, 7·2. $C_{19}H_{24}O_3N_2,C_2H_5{\cdot}OH$ requires C, 67·4; H, 8·1; N, 7·5%). The *hydrochloride* crystallises from water in anhydrous prisms, m. p. 300° (decomp.), $[\alpha]_D^{15°}$ + 201·0° (water) (Found: C, 63·0; H, 7·0; N, 7·3; Cl, 9·65. $C_{19}H_{24}O_3N_2,HCl$ requires C, 62·5; H, 6·9; N, 7·7; Cl, 9·7%).

The quantity of β-hydroxydihydro*apo*quinidine available is so small that its methylation has not been attempted.

Hydroxydihydroquinidine (III; Q = 6-methoxyquinolyl).—This substance occurs in the precipitation liquors obtained in the preparation of *iso*quinidines by the action of 70% sulphuric acid (p. 597). It was isolated by long-continued automatic extraction of the liquors with ether. The crude extract obtained, on solution in boiling acetone (1 g. in 2 c.c.), gave a crystalline crop, which was recrystallised twice from alcohol. The *base* separates from alcohol in small anhydrous prisms, m. p. 257°, $[\alpha]_D$ + 298·5° or + 225·3° (*c* = 1, alcohol) (Found: C, 70·6; H, 7·8; N, 8·2; MeO, 8·9. $C_{20}H_{26}O_3N_2$ requires C, 70·1; H, 7·6; N, 8·2; MeO, 9·1%). The hydrochloride crystallises from boiling absolute alcohol (1 g. in 3 c.c.) in prisms, m. p. 277° (decomp.), $[\alpha]_D^{15°}$ + 198·6°. This substance may be the methyl ether of β-hydroxydihydro*apo*quinidine.

Relative Stability of Quinidine Transformation Products to Potassium Permanganate.—To 5 c.c. of a 2% solution in water of the acid sulphate of the alkaloid, 0·3 c.c. of *N*-sulphuric acid was added, followed by 0·5 c.c. of *N*/50-potassium permanganate. With quinidine isomerides of types (I) and (VI), as well as with hydroxydihydroquinidine, the colour disappeared immediately; with isomerides of type (II) it was discharged in 3—3·5 minutes, and with dihydroquinidine the colour persisted for about 10 minutes.

Transformation Products of Quinine. Type (I).

The products of this type described already are *apo*quinine (Part I, p. 1927), its methyl ether, β-*iso*quinine (Part II, p. 968), and *isoapo*quinine (Part II, p. 967). The following account relates to experiments with the two last-mentioned substances.

Methylation of isoapo*Quinine to* α-iso*Quinine* (isoapo*Quinine Methyl Ether*).—*isoapo*Quinine gave with ethereal diazomethane in cold methyl-alcoholic solution a 44% yield of the crude methyl ether, which on recrystallisation from benzene or acetone (charcoal) formed glistening masses of colourless needles, m. p. 192—194° (with some sintering at 188—189°), $[\alpha]_D^{15°}$ − 364·3° or − 253·4° (alcohol) (Found: C, 74·3; H, 7·6; N, 8·45; MeO, 9·45. Calc. for $C_{20}H_{24}O_2N_2$: C, 74·0; H, 7·5; N, 8·6; MeO, 9·6%). These results leave no doubt of its identity with α-*iso*-quinine, for which Böttcher and Horowitz (*Monatsh.*, 1912, **33**, 567) record m. p. 196·5°, $[\alpha]_D^{18°}$ − 245° (c = 1) and − 248° (c = 0·5) in alcohol. In agreement with these authors' results the air-dry hydrochloride loses 2·3% on drying at 120° in a vacuum and re-gains 1·9% on exposure to air (Calc. for $C_{20}H_{24}O_2N_2$,HCl,1/3H_2O: H_2O, 1·6%. Found for dry substance: Cl, 9·8. Calc. for $C_{20}H_{24}O_2N_2$,HCl: Cl, 9·8%). The tartrate forms minute granules from aqueous alcohol as the alcohol is evaporated, and is less soluble in water or alcohol than β-*iso*quinine (*apo*quinine methyl ether) tartrate; m. p. 207—210° (corr., decomp.), $[\alpha]_D^{15°}$ − 206·5° (c = M/80; dry alcohol) [Found: C, 65·7; H, 7·1; N, 7·1. Calc. for $(C_{20}H_{24}O_2N_2)_2,C_4H_6O_6$: C, 66·1; H, 6·8; N, 7·0%].

Hydrogenation of β-iso*Quinine.* epi-C_3-*Dihydroquinine.*—β-*iso*Quinine, on catalytic hydrogenation in the manner described for the quinidine isomerides (p. 596), gave a crude product, m. p. 165°, $[\alpha]_D^{15°}$ − 255·7°, which after cleaning by a single crystallisation as the neutral sulphate, was freed from dihydroquinine by repeated crystallisation of the dihydrobromide from hot water, to constant optical rotation, $[\alpha]_D^{15°}$ − 184°, which is equivalent to − 275·4° for the base. The *dihydrobromide* crystallises in glistening colourless rosettes of flattened needles, which become bright yellow on drying in a vacuous desiccator and decolourise in a few minutes on re-exposure to air. The salt sinters from 225° and is completely decomposed at 234° (Found: loss on drying at 120° in a vacuum, 9·6. $C_{20}H_{26}O_2N_2$,2HBr,3H_2O requires loss, 9·9%. Found for dry salt: C, 49·5; H, 6·2; N, 5·6; Br, 32·4; MeO, 6·3. $C_{20}H_{26}O_2N_2$,2HBr requires C, 49·1; H, 5·8; N, 5·7; Br, 32·7; MeO, 6·3%).

The *base* recovered from the dihydrobromide crystallises on evaporation of the ether used for extraction and shows no change of m. p., 169°, on recrystallisation from benzene (Found for substance dried at 120° in a vacuum: C, 73·6; H, 8·2; N, 8·6. $C_{20}H_{26}O_2N_2$ requires C, 73·6; H, 8·0; N, 8·6%). As already pointed out (p. 593), this substance must be *epi*-C_3-dihydroquinine. Though the dihydrobromide provided a ready means of separating the isomeride of higher rotation, it was much less satisfactory for the isolation of the second component, since, like most salts of dihydroquinine except the sulphate, it was very soluble in water. By persistent recrystallisation of the middle fractions and accumulation of the ultimate residues a small fraction of slightly coloured but well-crystallised material was obtained having $[\alpha]_D^{16°}$ − 158·3°. Dihydroquinine dihydrobromide has $[\alpha]_D^{16°}$ − 157·5°. This and similar small fractions were mixed and converted into the neutral sulphate, which was obtained in the characteristic colourless, hair-like needles of dihydroquinine sulphate. The specimen lost 11·9% on drying in a vacuum at 120° and had $[\alpha]_D^{16°}$ − 206°, which is equivalent to $[\alpha]_D^{16°}$ − 237° for the base. Dihydroquinine sulphate, $(C_{20}H_{26}O_2N_2)_2,H_2SO_4,6H_2O$, requires loss on drying, 12·6% and has $[\alpha]_D$ − 204·6°, equivalent to − 235·4° for the base.

Hydrogenation of α-iso*Quinine.*—Reduction and the separation of the components were effected as described in the preceding paragraph. The initial base, purified through the sulphate, had $[\alpha]_D^{15°}$ − 253·8°. The dihydrobromide of highest rotation obtained had $[\alpha]_D^{16°}$ − 184·0° and agreed in characters with the *epi*-C_3-dihydroquinine dihydrobromide described above. The sulphate prepared from the ultimate mother-liquors had $[\alpha]_D^{15°}$ − 206·4° and had the characteristics of dihydroquinine sulphate.

Ozonisation of n-*Butyl*apo*quinine.*—A preliminary ozonisation experiment with *apo*quinine having given unpromising results, the experiment was repeated with *n*-butyl*apo*quinine, of

which a considerable quantity had been prepared for another purpose. The ether (3 g.) in chloroform (60 c.c.) was ozonised at 0° during 4½ hours. The yellowish product (3·3 g.) which separated during the operation was collected and hydrolysed with boiling water in an apparatus arranged for distillation; the distillate was collected in fractions, each of which was treated with *p*-nitrophenylhydrazine (cf. Reynolds and Robinson, J., 1934, 594). An orange-coloured crystalline precipitate formed in minute amount (0·05 g.). This had m. p. 118—122° after a single crystallisation from dilute alcohol. An authentic specimen of acetaldehyde-*p*-nitrophenylhydrazone had m. p. 124—127° and a mixture of the two had m. p. 121—125°. A second crystallisation failed to raise the m. p. (Found: C, 54·2; H, 5·4; N, 23·6. Calc. for acetaldehyde-*p*-nitrophenylhydrazone, $C_8H_9O_2N_3$: C, 53·6; H, 5·0; N, 23·5%. Calc. for formaldehyde-*p*-nitrophenylhydrazone, $C_7H_7O_2N_3$: C, 50·9; H, 4·25; N, 25·4%).

Transformation Products of Quinine. Type (III).

*Hydroxydihydro*apo*quinines* (*Hydroxydihydrocupreines*).—One of these isomerides has been described already (Part II, p. 968). It is proposed to distinguish that form as α-hydroxydihydro*apo*quinine. The process already described (Part I, p. 1927) for the isolation of the components of crude "apoquinine" has been improved by repeating the solution of the mixture in sodium hydroxide solution and reprecipitation by the passage of carbon dioxide several times, usually five. The final precipitate consists almost wholly of *apo*quinine and *isoapo*quinine, which can be separated by fractional crystallisation of the dihydrobromides from alcohol, in which the *apo*quinine salt is the less soluble, and from water, in which the *isoapo*quinine salt is the less soluble.

The hydroxydihydro*apo*quinines remain dissolved in the alkaline, carbonated precipitation liquors and are recovered by the following method. The liquors are neutralised with acid, concentrated to low bulk, again made alkaline, and treated with carbon dioxide until precipitation ceases. The filtrate is extracted with ether in a continuous-extraction apparatus, usually for 7 days, and the extract added to the precipitate. The product on solution in alcohol deposits α-hydroxydihydro*apo*quinine as already described (Part II, p. 968). The residual bases, on conversion into dihydrobromides, furnish a crystalline deposit from boiling alcohol, consisting largely of minute leaflets (A) suspended in the mother-liquor and a small quantity of crystalline crusts (B) adhering to the sides of the flask. Though product (A) is somewhat less soluble than (B), it has proved impossible to separate them by crystallisation, but fortunately they can readily be separated mechanically. They are both hydroxydihydro*apo*quinines and it is proposed to distinguish them as β- and γ-. The γ-isomeride has not yet been obtained in sufficient quantity for description.

β-*Hydroxydihydro*apo*quinine*.—The purification of the crude β-dihydrobromide is effected by repeated crystallisation from alcohol (10—15 times may be necessary) and is controlled polarimetrically. The base remains dissolved when liberated from solutions of its salts even under conditions which usually lead to precipitation of phenolic bases. Its recovery can be effected as follows. The dihydrobromide, dissolved in water, is poured into a known slight excess of a solution of sodium hydroxide, and *N*-hydrochloric acid carefully added; precipitation begins after the known excess of alkali is neutralised but before the whole of the sodium presumably in combination with the phenolic base has been converted into sodium chloride; and the careful addition of *N*-hydrochloric acid is continued until precipitation ceases. The precipitate is filtered off, and the rest of the base recovered by extraction of the filtrate in a continuous-extraction apparatus. The *base* so recovered is dried, packed in a Soxhlet apparatus, and extracted by dry ether; it gradually accumulates in the flask as a buff-coloured, amorphous powder, which is very sparingly soluble in all ordinary solvents except alcohol. It melts indefinitely, and after some effervescence at about 120°, and has $[\alpha]_D^{15°}$ − 205·1°. The base loses 4·1% on drying in a vacuum at 95° and regains 2·9% on re-exposure to air (Found for dry base: C, 69·0; H, 7·85; N, 8·0. $C_{19}H_{24}O_3N_2$ requires C, 69·45; H, 7·4; N, 8·5%).

The *dihydrobromide* crystallises from alcohol or water in glistening, greyish or cream-tinted rectangular plates. It begins to decompose at 235° and froths at 245°, has $[\alpha]_D^{15°}$ − 141·9°, and is readily soluble in water, sparingly in alcohol (Found for substance dried at 110° in a vacuum: C, 47·15; H, 5·65; N, 5·6; Br, 31·5. $C_{19}H_{24}O_3N_2$,2HBr requires C, 46·5; H, 5·35; N, 5·7; Br, 32·6%). The salt is deficient in bromine, as has been noticed with other dihydrobromides in this series. The *hydrochloride* crystallises from alcohol in small, colourless needles. It darkens from about 200°, shrinks at about 240°, and froths at 255° to 260°. The salt becomes slightly discoloured on drying in a vacuum at 120° and loses less than 1% by weight (Found: C, 62·5; H, 6·9; N, 7·4; Cl, 9·7. $C_{19}H_{24}O_3N_2$,HCl requires C, 62·5; H, 6·9; N, 7·7; Cl, 9·7%).

The *sulphate* crystallises from a concentrated aqueous solution in yellowish leaflets; it melts in its own water of crystallisation below 100°, but the dry salt has m. p. 265—270° (decomp.) [Found: loss on drying in a vacuum at 120°, 16·8. $(C_{19}H_{24}O_3N_2)_2,H_2SO_4,8·5H_2O$ requires loss, 16·9%. Found for dry salt: C, 60·4; H, 6·8; N, 7·25; S, 4·1. $(C_{19}H_{24}O_3N_2)_2,H_2SO_4$ requires C, 60·45; H, 6·7; N, 7·4; S, 4·3%]. The *d-tartrate*, $B_2,C_4H_6O_6$, separates from water in colourless needles with $2H_2O$ or from alcohol with $1C_2H_6O$. It decomposes at 235—240° and has $[\alpha]_D^{15°}$ – 99·5° (c = 0·5, alcohol). The acid dianisoyltartrate, $B,C_{20}H_{18}O_{10}$, crystallises from alcohol in colourless needles, m. p. 194—197° (decomp.), $[\alpha]_D^{15°}$ – 141·5° (c = 0·24, alcohol). The base could not be hydrogenated catalytically and on treatment with diazomethane gave an amorphous product, with a small amount of a crystalline substance, which appeared to be a quaternary compound.

*Methylation of α-Hydroxydihydro*apo*quinine* (Part II, p. 968).—The crude product resulting from the interaction of α-hydroxydihydro*apo*quinine (5 g.) in methyl alcohol (200 c.c.) and diazomethane (*ex* nitrosomethylurethane, 10 c.c.) in ether (125 c.c.) during 2 hours was crystallised once from alcohol–acetone to remove some tar, and then worked up as usual, being finally crystallised from boiling methyl alcohol. The *base* separated in felted, lustrous masses of needles, m. p. 247—249° (corr.), $[\alpha]_D^{15°}$ – 197·5° or – 119·1° (c = M/40, dry alcohol). It is almost insoluble in ether, benzene, or chloroform but dissolves in hot ethyl alcohol, the solution gelatinising on cooling (Found for substance dried at 120° in a vacuum: C, 70·2; H, 7·6; N, 8·1; MeO, 9·1. $C_{20}H_{26}O_3N_2$ requires C, 70·1; H, 7·7; N, 8·2; MeO, 9·1%). The *hydrochloride* crystallises from dilute methyl alcohol in silky needles, m. p. 255—259° (corr., decomp.), $[\alpha]_D^{15°}$ – 94·6° (c = M/40, dry alcohol) (Found: loss on drying at 120° in a vacuum, 10·5. $C_{20}H_{26}O_3N_2,HCl,2·5H_2O$ requires H_2O, 10·6%. Found for dry substance: C, 63·3; H, 7·2; N, 7·3; Cl, 9·4; MeO, 7·8. $C_{20}H_{26}O_3N_2,HCl$ requires C, 63·4; H, 7·2; N, 7·4; Cl, 9·4; MeO, 8·2%). The *nitrate* crystallises from boiling water (1 g. in 20 c.c.) in matted, long needles, m. p. 226° (corr., decomp.) with previous sintering, $[\alpha]_D^{15°}$ – 103·8° (c = M/40, dry alcohol) (Found: loss on drying at 120° in a vacuum, 4·0. $C_{20}H_{26}O_3N_2,HNO_3,H_2O$ requires H_2O, 4·2%. Found for dry substance: N, 9·9. $C_{20}H_{26}O_3N_2,HNO_3$ requires N, 10·4%).

The results of protozoicidal and bactericidal tests with these substances and an extensive series of *apo*quinine ethers, for which we are indebted to Drs. Trevan and Buttle of the Wellcome Physiological Research Laboratories, will be published in full elsewhere, but it may now be pointed out that, whereas isomerides of type (I) have in general anti-malarial action comparable in kind and degree with that of the parent alkaloids (type IV), isomerides of type (II) and the hydration products (type III) exhibit no anti-malarial activity.

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134. *An Oxidation Product of Adrenaline.*

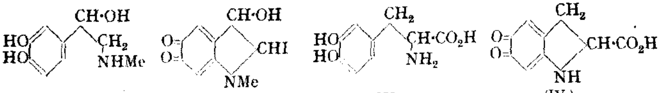
By DEREK RICHTER and HERMANN BLASCHKO.

ADRENALINE gives a deep red coloration when an aqueous solution is treated with potassium iodate solution (Fränkel and Allers, *Biochem. Z.*, 1909, **18**, 40; Kraus, *ibid.*, 1909, **22**, 131). The reaction has been used in histological work for staining tissues containing adrenaline and for the colorimetric estimation of adrenaline. A similar red coloration is given with a number of other oxidising agents and in the oxidation catalysed by tissue extracts (Green and Richter, *Biochem. J.*, in the press), but the oxidation products are very unstable and nothing is known of their chemical nature.

The red product formed when adrenaline (I) is oxidised with potassium iodate has now been isolated and found to have the properties of 2-iodo-3-hydroxy-1-methyl-2 : 3-dihydroindole-5 : 6-quinone (II).

The ring closure to give an indole derivative on oxidation in dilute aqueous solution can be compared with the ring closure which Raper found to take place under similar

conditions with dihydroxyphenylalanine (III) (*Biochem. J.*, 1927, **21**, 89). The product was in this case the dihydroindolequinone-2-carboxylic acid (IV).



(I.) (II.) (III.) (IV.)

EXPERIMENTAL.

l-Adrenaline (50 mg.) in 1 c.c. of 2% acetic acid was treated with 2 c.c. of 4% potassium iodate solution. The mixture went deep red and the product (75 mg.) slowly separated in prisms with a green metallic glance. Back titration of the excess of iodate showed that 57 mg. of potassium iodate were used in the reaction (calc. for 1 mol. per mol. of adrenaline, 58 mg.). The solution contained no iodide at the end of the reaction. A reaction was therefore indicated according to the equation

$$C_9H_{13}O_3N,CH_3{\cdot}CO_2H + KIO_3 \longrightarrow C_9H_8O_3NI + CH_3{\cdot}CO_2K + 3H_2O$$

This formula for the reaction product was confirmed by microanalysis (Found: C, 36·3; H, 2·7; N, 4·8; I, 40·4. $C_9H_8O_3NI$ requires C, 35·4; H, 2·6; N, 4·6; I, 41·6%).

The substance was very unstable. In the crystalline condition it decomposed after a few weeks. On heating, it decomposed without melting at about 150°. It was only very sparingly soluble in water, sparingly soluble in alcohol, and insoluble in most other solvents. The aqueous solution decomposed rapidly on treatment with dilute acid or alkali or on boiling.

The red colour of the compound suggested that it was quinonoid. This was confirmed by the fact that it was easily reduced by sulphur dioxide or magnesium powder and acetic acid; the colourless phenolic product gave, with ferric chloride, the green colour, changing to red on addition of ammonia, which is characteristic of a catechol derivative. The phenolic compound was optically active; a 1·15% solution obtained by reducing the quinone with sodium sulphite gave $[\alpha]_D^{18°} = +154°$. This indicated that the oxidation had not affected the asymmetry of of the CH·OH group.

Both the red quinone and its reduction product were much less basic than adrenaline, being insoluble in 5% acetic acid. On warming with 5% hydrochloric acid, the substance decomposed, forming free iodine, which could be extracted with chloroform. The ease with which iodine was formed made it likely that the iodine was substituted in the side chain rather than in the benzene nucleus.

Examination of the ultra-violet absorption spectrum of the reduction product showed that it gave a maximum at approximately 3800 A. The spectrum in the 2000—4000 A. region was of a different type from that given by adrenaline and other catechol derivatives. Since the absorption spectrum in this region is determined largely by the nature and number of the substituents in the benzene nucleus, this indicated that substitution in the benzene nucleus had probably occurred.

Ball and Chen obtained evidence by means of potentiometric measurements that the primary product formed when adrenaline is oxidised by a number of different oxidising agents is generally the corresponding *o*-quinone (*J. Biol. Chem.*, 1933, **102**, 702). The formula $C_9H_8O_3NI$ contains two hydrogen atoms less than an iodinated *o*-quinone of adrenaline. That means that two hydrogen atoms have been removed in a reaction which rendered the nitrogen atom less basic and at the same time brought about a substitution in the benzene nucleus. The simplest explanation is that ring closure between the nitrogen atom and the benzene nucleus to give a dihydroindole derivative had occurred. *o*-Quinones are known to condense with amines to give red amino-quinones (Jackson and Koch, *Ber.*, 1898, **31**, 1459). An intramolecular condensation of the type suggested is therefore not improbable.

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CAMBRIDGE. [*Received, March 8th, 1937.*]

135. *Catalytic Toxicity and Chemical Structure. Part I. The Relative Toxicity of Sulphur Compounds in Catalytic Hydrogenation.*

By Edward B. Maxted and Herbert C. Evans.

The variation of catalytic toxicity with the structure of the inhibitant is of considerable interest in connection with the method and degree of attachment of a poison to a catalytic surface. Unlike most adsorbed species, a poison—by virtue of its negligible rate of evaporation and, consequently, its obstructive occupation of surface—becomes attached permanently to at least one surface element by a linkage involving the poisonous element contained in its molecule. If the inhibitant in question contains, for instance, a residual non-poisonous chain of any length, although this chain may be of a structure such that in the absence of the poisonous element or group it would normally be freely adsorbed and evaporated, it may—by reason of the permanent attachment at one point—itself be in a preferential position for further attachment, in that the free evaporation of the molecule as a whole is inhibited; and, in this way, the permanent linkage at one point may cause a remaining, normally non-poisonous portion of the molecule to become toxic. This point will be discussed in the course of the following work, in which the toxicity or power of covering of a poison containing, for instance, one sulphur atom will be seen to be increased by the introduction of a normally non-poisonous chain or ring.

It has been considered of interest, as a first stage, to investigate quantitatively the relative toxicity of various types of sulphur compounds which commonly occur in substances ordinarily subjected to catalytic hydrogenation, the present work being preliminary to a more systematic investigation of the effect of structure and of chain length on toxicity, namely, on the effective power of covering of an inhibitive molecule attached to a surface by a permanently linked point. From the standpoint of practical hydrogenation, the principal types of sulphur compounds which occur in the impure substances normally employed include cyclic thio-compounds—typified by thiophen and its analogues—and, especially in products such as unsaturated glycerides, albuminoid sulphur together with albuminoid decomposition products, which may be represented by sulphur-containing amino-acids such as cysteine and, as a stage further, by hydrogen sulphide. Accordingly, in the present paper, the relative toxicity of hydrogen sulphide, carbon disulphide, thiophen, and cysteine, also of elementary sulphur, towards a platinum and a nickel catalyst, has been measured.

The sensitivity of a given catalyst to a given poison varies greatly with its degree of subdivision, a coarse-grained, relatively inactive catalyst being far more sensitive to poisoning than a finely-divided, highly active one, especially if the fineness of subdivision be increased and stabilised by the use of a carrier. For this reason, two widely differing preparations, *viz.*, a relatively coarse platinum and a far more finely-divided supported nickel catalyst, were taken, the ratio of the sensitivity towards a given poison of the former to the latter catalyst being of the order of fifty to one.

It is of interest to note that—in spite of the above wide difference in sensitivity to an individual poison—not only was the sequence of the above series of inhibitants, in order of increasing toxicity, the same for both catalysts, but also the relative toxicities of the inhibitants, *viz.*, the ratio of the toxicity of a given sulphur compound to that of another, expressed quantitatively per unit of sulphur, were found to be very similar for both metals; further, the toxicity of the poison per unit of sulphur increases in each case with the complexity of the chain or ring attached to the sulphur.

Experimental.

The platinum used was prepared by Mond, Ramsay, and Shields's method (*Phil. Trans.*, 1895, *A*, **186**, 657), *i.e.*, by the reduction of chloroplatinic acid with an alkaline formate, followed by prolonged washing. It was subsequently heated to 200° to ensure stability on storage and in use. The resulting catalyst possessed a high degree of sensitivity to poisons and could be stored, at any rate for several weeks, without measurable deterioration. The nickel was made by reduction with hydrogen of nickel carbonate on a kieselguhr support. In this

case also, for reasons of stability, the maximum possible activity was not aimed at. Accordingly, although this nickel was far less sensitive to poisoning than the platinum, it was more sensitive than an ordinary supported nickel catalyst for which permanence in activity on storing is not necessary. It was stored in stearin. Both with nickel and with platinum, the catalyst required for each measurement was taken from the same stock throughout; and each charge of catalyst was only used once.

For the measurement of the activity of each catalyst at various stages of poisoning, the general method already described (J., 1921, **119**, 225; 1935, 393, 1190) was employed, the toxicity being expressed in the form of the poisoning coefficient (J., 1934, 26, 672), *viz.*, as the coefficient, α, in an expression of the type $k_c = k_0(1 - \alpha c)$, in which k_c is the activity of the catalyst in the presence of a concentration, c, of the poison, and k_0 is the original, unpoisoned activity. It has previously been found that this expression holds for the greater part of the poisoning curve, probably up to a stage beyond which the bulk concentration of poison present begins to be too high to be substantially completely adsorbed (see J., 1925, **127**, 73) by the amount of catalyst used: indeed, in the present work, care was taken—by testing the decanted, originally poisoned supernatant liquid for freedom from poison after allowing the catalyst to settle—that the conditions were such that the poison added was completely adsorbed by the catalyst and that the adsorbed poison content was thus that represented by the bulk concentration of poison originally added. The poisons themselves were either already available in a pure condition or were carefully purified. Thus, the specimen of carbon disulphide used was sufficiently free from other sulphur compounds to possess an ethereal odour. In the case of hydrogen sulphide, which was made from magnesium hydrosulphide, it was necessary to carry out the toxicity measurements immediately after the preparation of the standard poisoning solution in order to avoid a change with time in the concentration and form of the poison in the very dilute solutions employed.

The usual precautions were taken to ensure the constancy of the rate of presentation of hydrogen and unsaturated substance at the catalytic surface. For instance, the standard conditions of agitation were maintained throughout each of the series by employing the same shaking vessel, driven at a constant, relatively high rate. Accordingly, since the same solvent and unsaturated substance were used, the conditions were identical save for the presence of the poison. This constancy of the external conditions was confirmed by duplicate tests both with the unpoisoned catalysts and with these in a known poisoned state. As a still further precaution—in view of the extremely small quantities of poison involved (of the order of 0·01—0·04 mg. in the case of platinum)—duplicate measurements involving a fresh weighing out of the poison and the preparation, by dilution, of an independent standard solution were also carried out. These agreed well in each case with those of the main series.

Relative Toxicity towards Platinum.—The series of inhibitants taken was elementary sulphur (which is slightly, but sufficiently, soluble in glacial acetic acid), hydrogen sulphide, carbon disulphide, thiophen, and cysteine. Crotonic acid was used as a standard unsaturated substance for hydrogenation; and the system contained in each case 0·05 g. of platinum, 10 c.c. of a *N*-solution of crotonic acid in glacial acetic acid, and the required quantity of the poison dissolved in a further 10 c.c. of acetic acid. The effect of various quantities of the above inhibitants on the activity of the platinum is shown in Fig. 1, the sulphur content of the system being expressed in g.-atoms of sulphur, which is equivalent to the content, in g.-mols., of the inhibitant itself, save in the case of carbon disulphide, which possesses two potentially linking sulphur atoms. Elementary sulphur also is included on the basis of the toxicity per g.-atom. The temperature employed was in each case 27°.

It will be seen that the toxicity per unit of sulphur increases with the molecular weight of the inhibitant, *i.e.*, with the complexity of the chain or ring attached to the sulphur. From the slope of the poisoning graph, the following values are obtained for α, the poisoning coefficient in respect of the catalytic surface represented by the standard amount (0·05 g.) of the platinum preparation taken, the concentration of the inhibitant being expressed as above:

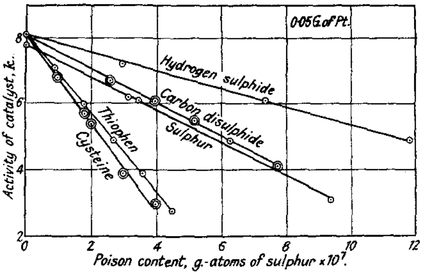
Inhibitant.	Mol. wt.	$\alpha \times 10^{-5}$.	Relative toxicity per g.-atom of S.
Hydrogen sulphide	34	3·4	1
Sulphur	$(32)_n$	6·4	1·9
Carbon disulphide	76	6·4	1·9
Thiophen	84	14·8	4·4
Cysteine	121	16·7	5·0

Relative Toxicity towards Nickel.—Since hydrogenation reactions with nickel are usually carried out at a higher temperature than with platinum, crotonic acid in acetic acid solution

cannot conveniently be used as the standard unsaturated substance for the measurement of activity. Accordingly, olive oil, previously purified by the usual fuller's earth and soda treatment, was substituted. The system taken for each measurement consisted of 0·05 g. of nickel, which was added as a suspension in stearin, and 10 c.c. of olive oil, including that added with the poison, which was in each case made up in standard olive oil solution. All materials were taken from the same stock throughout the whole of the work. The temperature employed was 160°. At this high temperature, the linear reaction path, corresponding with a process of zero order—which is normally followed in the hydrogenation of pure substances at low temperatures both in the absence and in the presence of an added poison, and which results in an approximately constant hydrogenation velocity during, at any rate, not too advanced stages of the hydrogenation—becomes curved (*J. Soc. Chem. Ind.*, 1921, **40**, 169T); and the velocity of hydrogenation decreases with the time. During early stages of the hydrogenation of an oil,

FIG. 1.

The relative toxicity of sulphur compounds in catalytic hydrogenation.



the deviation from a linear path is, however, not great; and the slight curvature may be allowed for by differentiating for zero time the equation to the absorption–time curve. The figure obtained represents the initial velocity of absorption of hydrogen, and may be conveniently employed as a measure of the activity of the nickel under conditions in which a zero-order hydrogenation path is not followed.

Save for the omission of elementary sulphur, the series of inhibitants studied was the same as for platinum. The variation of the activity of 0·05 g. of nickel with the poison content is summarised in Fig. 2. In this, the widely differing general sensitivity to poisoning between the coarse-grained platinum catalyst and this supported nickel catalyst is emphasised by the difference in the scale of the axis representing the poison content, which is 100 times as large (g.-atoms of S × 10^{-5}) as that of Fig. 1 (g.-atoms of S × 10^{-7}); but the inhibitants fall in the same sequence of toxicity as for platinum. The higher toxicity of carbon disulphide, compared with hydrogen sulphide, is in agreement with Kelber's observation (*Ber.*, 1916, **49**, 1868).

The poisoning coefficients for this preparation of nickel are given in the following table, in which the relative toxicities previously found for platinum have been included for purposes of comparison. It will be seen that, in spite of the wide difference in general sensitivity of the two

Inhibitant.	$\alpha \times 10^{-3}$.	Relative toxicity per g.-atom of S.	Relative toxicity towards Pt.
Hydrogen sulphide......	7·5	1	1
Carbon disulphide	18·2	2·4	1·9
Thiophen	33·3	4·5	4·4
Cysteine	40·0	5·4	5·0

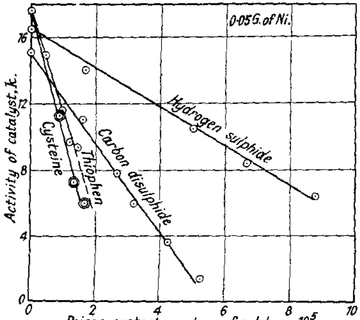
catalysts, the relative toxicity of the various poisons one to another is almost identical for nickel and for platinum.

If relative toxicity is regarded as a measure of relative obstructive covering power of a potentially catalytically active range of surface elements by a poison, this similarity in relative toxicity towards nickel and platinum might be expected on grounds of the similar-

ity in magnitude of the lattice constants of nickel and platinum (3·5 and 3·9 A., respectively). The effective lengths, in similar units, of the bonds involved in the structure of the various inhibitants is also well known on the basis of *X*-ray and other evidence; and it should thus be possible to reproduce the probable power of covering of a given structure by the superimposition of scale models of the inhibitants on to a model of the crystal lattice involved. It is hoped to deal with this point in greater detail in a later paper. It appears, further,

FIG. 2.

The relative toxicity of sulphur compounds in catalytic hydrogenation.



not impossible that relative data for power of covering may—if an inhibitant of known chain length can be used as what may be regarded as a molecular measuring scale—be made to yield evidence on the distance apart of catalytically active surface elements and on the identity or otherwise of this distance with that separating the normal lattice atoms of the catalyst. This information is of considerable interest in connection with the existence and nature of so-called active points on a catalytic surface.

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136. *Equilibrium Constants in Terms of Activities (Cryoscopic). Part VI. Pyridine* p-*Chlorophenoxide in Benzene and in* p-*Dichlorobenzene.*

By W. R. BURNHAM and W. M. MADGIN.

THE freezing point–composition diagram for the system pyridine–*p*-chlorophenol exhibits a very sharp maximum at the point corresponding to the compound pyridine *p*-chlorophenoxide, which shows pronounced super-cooling (J., 1936, 789). These facts suggest that the compound has marked stability, and therefore the equilibrium constants of its dissociation in benzene and in *p*-dichlorobenzene have been determined by the methods already described (J., 1936, 1303, and earlier references). The exceptionally small heat of formation of the compound is discussed.

Purification of materials and the experimental cryoscopic method were as before (*loc. cit.*). The table and the figure give the results of the present work.

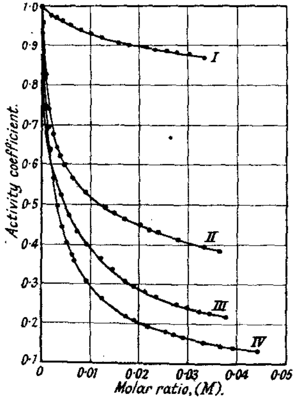
Heat of Formation.—The average values of K_a (table) have been applied in the isochore (cf. Part II, J., 1933, 1431), whence the heat of formation of pyridine *p*-chlorophenoxide has been found to be $Q = -480$ cals., the compound being formed exothermally.

***Equilibrium constants and activity coefficients for benzene and* p*-dichlorobenzene solutions of pyridine* p*-chlorophenoxide at molar ratio* = M.**

(γ_A, γ_B, γ_{AB} = activity coefficient of pyridine, *p*-chlorophenol, and undissociated pyridine *p*-chlorophenoxide, respectively.)

$10^3 \times M$.	ΔT.	K_e.	γ.	γ_A.	γ_B.	γ_{AB}.	$10^3 \times M$.	ΔT.	K_e.	γ.	γ_A.	γ_B.	γ_{AB}.
				(a) *Benzene solutions.*									
0·510	0·061°	443·8	0·838	0·957	0·997	0·993	12·38	0·927°	444·1	0·262	0·852	0·973	0·528
0·960	0·109	446·0	0·747	0·939	0·994	0·984	17·43	1·241	444·9	0·219	0·839	0·967	0·494
1·364	0·149	442·1	0·691	0·925	0·992	0·950	19·05	1·341	446·0	0·208	0·836	0·966	0·475
1·701	0·179	444·0	0·640	0·922	0·991	0·945	21·76	1·500	443·5	0·194	0·831	0·963	0·465
2·301	0·225	444·0	0·565	0·912	0·990	0·837	25·22	1·701	442·2	0·179	0·827	0·961	0·448
3·218	0·296	441·0	0·493	0·906	0·986	0·735	27·14	1·812	443·2	0·172	0·824	0·960	0·438
4·114	0·362	442·5	0·441	0·902	0·984	0·689	29·08	1·919	442·8	0·165	0·819	0·958	0·433
5·103	0·440	442·7	0·400	0·883	0·982	0·644	33·79	2·173	444·0	0·151	0·815	0·956	0·413
6·131	0·514	443·6	0·372	0·880	0·980	0·623	36·55	2·323	443·6	0·144	0·812	0·955	0·403
6·676	0·549	446·4	0·355	0·878	0·979	0·607	39·06	2·454	444·3	0·138	0·810	0·954	0·392
9·092	0·711	444·4	0·305	0·862	0·977	0·565	41·98	2·607	446·4	0·133	0·806	0·952	0·389
				(b) p-*Dichlorobenzene solutions.*									
1·484	0·121	393·2	0·708	1·004	1·000	0·990	21·80	1·311	394·3	0·275	1·057	0·972	0·910
2·874	0·217	394·1	0·614	1·014	0·996	0·985	24·28	1·443	394·2	0·262	1·060	0·971	0·906
4·352	0·304	392·1	0·514	1·028	0·992	0·980	28·13	1·646	396·9	0·246	1·064	0·968	0·897
6·061	0·417	393·4	0·465	1·034	0·991	0·973	30·20	1·752	395·4	0·225	1·068	0·966	0·893
7·877	0·524	396·0	0·425	1·040	0·986	0·965	32·89	1·893	392·1	0·223	1·070	0·964	0·887
9·749	0·639	392·3	0·391	1·044	0·985	0·953	35·10	2·003	394·2	0·220	1·071	0·962	0·882
12·52	0·800	394·1	0·356	1·048	0·982	0·941	38·11	2·151	394·1	0·211	1·074	0·958	0·877
15·20	0·951	394·0	0·330	1·053	0·978	0·930	42·33	2·362	392·7	0·195	1·076	0·954	0·869
17·73	1·092	394·0	0·300	1·056	0·976	0·923							

Average values of K_e: in benzene, 443·8; in *p*-dichlorobenzene, 394·0.



I and III, dichlorobenzene solutions.
II and IV, benzene solutions.
I and II, undissociated pyridine *p*-chlorophenoxide (γ_{AB}).
III and IV, pyridine and *p*-chlorophenol together in solution (γ).

Discussion.

The present values of K_a are much larger than those previously reported (*loc. cit.*) for other amine–phenol compounds, particularly in *p*-dichlorobenzene solutions. This indication of considerable stability in pyridine *p*-chlorophenoxide might be expected from a consideration of the dipole moments of the components of the compound, *viz.*, pyridine, 2·2; *p*-chlorophenol, 2·3 (*Trans. Faraday Soc.*, **1934**, **30**, Appendix), but, contrary to expectation, the heat of formation ($Q = -480$ cals.) is much less than any of those reported previously; compare especially pyridine *o*-chlorophenoxide, $Q = -6800$ cals. (Part II, J., **1933**, **1431**). The difference between these two heat values can scarcely be ascribed to some special property of *p*-chlorophenol, since the corresponding chlorophenoxides of

p-toluidine have heats of formation which do not greatly differ (Part V, J., **1936**, 1302). Marked differences in heats of formation of amine–phenol compounds do not seem to accord with the idea that a well-defined link, N→H, is formed in all such compounds (cf. Part IV, J., 1934, 1292).

The properties of benzene and *p*-dichlorobenzene were discussed (Part II, *loc. cit.*), and it was considered that these two substances were solvents which provide similar thermodynamic environments. Hence specific solvent influences, as a cause of very small heat effects, are assumed to be of a very subsidiary nature. An examination of the data reported in earlier parts of the present series of papers reveals no evidence of such specific influences.

The relative lengths of the dipoles of component molecules in compounds may be expected to influence the type of combination and hence the heats of formation. Bernal (*Trans. Faraday Soc.*, 1934, **30**, 776), considering the association of alcohols, suggested that two types of complex may be formed, *viz.*, polar and non-polar. A similar difference may exist between pyridine *p*-chlorophenoxide and its *o*-chlorophenoxide, the former being a polar compound. The very different dipole lengths of *p*-chlorophenol and pyridine may account for the formation of such a polar compound, which, in turn, may account for the small heat of formation of pyridine *p*-chlorophenoxide now reported. Such explanation is speculative, and a precise interpretation of the results in this series of papers cannot be put forward at present.

SUMMARY.

The equilibrium constant, $K_a = a_{AB}/a_A a_B$, has been calculated for the dissociation of pyridine *p*-chlorophenoxide in benzene and in *p*-dichlorobenzene solutions. Average values of K_a have been found for the two mean temperatures, $T = 277·0°$ and $T = 324·3°$, and the van't Hoff isochore has been applied to calculate the heat of formation of pyridine *p*-chlorophenoxide. This heat of formation is quite small compared with those previously reported, and a possible explanation has been discussed.

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137. *Acid Salts of Monobasic Organic Acids. Part III.*

By JOHN D. M. ROSS, THOMAS J. MORRISON, and CECIL JOHNSTONE.

THE extent of compound formation which takes place between *r*-mandelic acid and various metal mandelates has already been studied by Ross and Morrison (J., 1933, 1016; J., 1936, 867). In the present investigation similar systems have been studied, active mandelic acid and active metal mandelates being used.

EXPERIMENTAL.

(−)*Mandelic Acid.*—The (−)mandelic acid used was prepared by (*a*) hydrolysis of amygdalin with concentrated hydrochloric acid; (*b*) resolution of *r*-mandelic acid with morphine (McKenzie, J., 1899, **75**, 966; Wood, Chrisman, and Nicholas, J., 1928, 2186), and (*c*) with (−)ephedrine (Roger, J., 1935, 1544). The average value of the specific rotation of the acid in water (1% solution) was $[\alpha]_D^{14°} = -154°$.

Metal Mandelates.—The active mandelates were in most cases prepared in exactly the same manner as the inactive salts, but in dealing with thallous, rubidium, and cæsium mandelates modifications in procedure were introduced which are described below.

The specific rotations of the salts in aqueous solution ($l = 2$) were:

(−)Mandelate.	*c.*	*a.*	*t.*	$[\alpha]_D^{t°}$.
Lithium	1·0	−2·32°	14°	−116°
Sodium	1·037	−2·17	12	−104·6
Potassium	1·017	−1·90	20	− 93·4
Magnesium (hydrated)	1·0	−2·07	14	−103·5
,, (anhydrous)	1·008	−2·28	15	−113·2
Calcium	1·006	−2·24	15	−111·4
Strontium	1·003	−1·19	15	− 95·3
Barium (hydrated)	1·0	−1·64	15	− 81·75
Thallous	1·015	−1·00	14	− 49·26

Thallous (−)Mandelate.—This salt was prepared with difficulty. 32·5 G. of (−)mandelic acid, dissolved in 200 c.c. of water, were neutralised with 50 g. of thallous carbonate, but only a gum was produced on attempted crystallisation of the product from aqueous methyl alcohol, although the inactive salt readily crystallised from this solvent: other solvents gave no better results. Finally, a crystalline salt was obtained by the following procedure. 3·25 G. of (−)mandelic acid were melted in a platinum basin at 140°, 5 g. of thallous carbonate added, and the mixture kept for a few minutes at this temperature before being cooled in a desiccator. The solid obtained was used to seed the gum obtained in the previous attempt, and a crystalline non-deliquescent material was formed.

Rubidium and Cæsium (−)Mandelates.—The method used for the inactive salts failed to give crystallisable material. Solutions for analysis were prepared by adding appropriate amounts of mandelic acid to weighed amounts of rubidium and cæsium carbonates.

The analytical data for the foregoing salts are included in the table on p. 614.

1. *The System (−)Mandelic Acid–Lithium Mandelate–Water.*—The solid phase was separated for analysis by pressing and drying on a porous plate.

Lithium (−)mandelate.

Solution.			Solution.			Solution.		
Acid, %.	Salt, %.	Solid phase.	Acid, %.	Salt, %.	Solid phase.	Acid, %.	Salt, %.	Solid phase.
10·1	0·0	Acid	11·9	3·4	1 : 1-Acid salt	6·9	4·0	1 : 1-Acid salt
9·8	0·5	,,	10·6	3·5	,,	5·6	4·0	,,
9·9	0·8	,,	10·8	3·4	,,	2·6	5·6	,,
10·0	1·7	,,	11·0	3·4	,,	1·3	8·6	Normal salt
10·1	2·0	,,	10·6	3·5	,,	1·0	8·5	,,
10·2	2·6	,,	9·9	3·6	,,	0·0	8·6	,,
10·3	3·4	,,	9·2	3·7	,,			

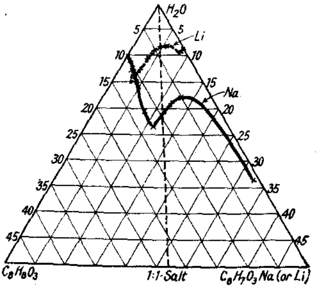
2. *The System (−)Mandelic Acid–Sodium Mandelate–Water.*—The solid phase for analysis was dried on a porous plate.

Sodium (−)mandelate.

Solution.		Residue.		Solution.		Residue.	
Acid, %.	Salt, %.	Acid, %.	Solid phase.	Acid, %.	Salt, %.	Acid, %.	Solid phase.
10·1	0·0	—	Acid	12·3	11·3	90·9	Acid + 1 : 1-salt
10·0	0·9	—	,,	8·9	11·6	46·5	1 : 1-Acid salt
10·1	1·7	—	,,	7·4	11·9	46·1	,,
11·0	4·3	—	,,	5·1	13·0	—	,,
11·2	5·0	—	,,	0·8	32·6	44·3	,,
12·2	8·5	97·7	,,				

FIG. 1.

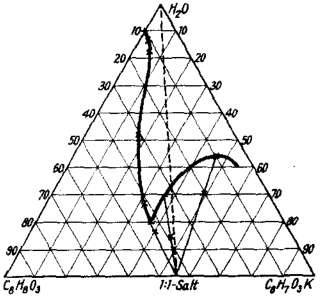
Lithium and sodium mandelates.



Both acid salts stable.

FIG. 2.

Potassium mandelate.



Acid salt stable.

3. *The System (−)Mandelic Acid–Potassium Mandelate–Water.*—The solid phase was determined by the residue method.

Potassium (—)mandelate.

Solution.			Solution.		Residue.		
Acid, %.	Salt, %.	Solid phase.	Acid, %.	Salt, %.	Acid, %.	Salt, %.	Solid phase.
10·1	0·0	Acid	39·8	27·2	—	—	Acid + 1 : 1-salt
10·1	1·4	,,	42·7	37·3	43·6	40·4	1 : 1-Acid salt
10·5	3·2	,,	34·4	38·5	39·1	46·7	,,
12·1	6·0	,,	9·7	46·4	20·2	49·6	,,
30·9	17·7	,,					

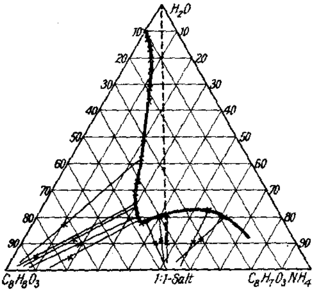
4. *The System (—)Mandelic Acid–Ammonium Mandelate–Water.*— Schreinemakers's residue method was used in the analysis of the solid phase, owing to the very viscous solutions obtained at higher concentrations.

Ammonium (—)mandelate.

Solution.		Residue.			Solution.		Residue.		
Acid, %.	Salt, %.	Acid, %.	Salt, %.	Solid phase.	Acid, %.	Salt, %.	Acid, %.	Salt, %.	Solid phase.
10·1	0·0	—	—	Acid	46·0	30·9	—	—	Acid
10·1	2·3	—	—	,,	46·5	34·0	71·1	17·6	,,
11·3	5·1	—	—	,,	46·8	34·8	76·3	18·4	,,
12·9	7·8	—	—	,,	47·2	35·4	—	—	,,
15·0	10·1	—	—	,,	46·9	36·0	—	—	,,
18·8	13·1	—	—	,,	43·9	36·4	45·9	43·7	1 : 1-Acid salt
21·1	15·1	—	—	,,	38·3	40·2	44·0	44·5	,,
31·1	19·5	—	—	,,	37·0	42·6	42·3	47·1	,,
33·8	22·9	72·7	14·4	,,	29·0	48·0	—	—	,,
39·1	25·9	—	—	,,	24·7	51·9	—	—	,,
40·3	26·4	—	—	,,	22·2	55·5	33·6	56·9	,,
41·2	27·4	—	—	,,	19·0	61·0	30·2	57·8	,,
44·3	27·6	88·2	7·2	,,	18·7	61·5	—	—	,,
45·8	30·6	71·7	16·5	,,					

FIG. 3.

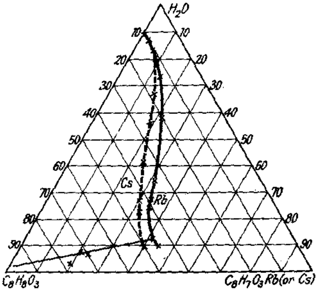
Ammonium mandelate.



Acid salt stable.

FIG. 4.

Rubidium and cæsium mandelates.



No acid salts formed.

5. *The System (—)Mandelic Acid–Rubidium Mandelate–Water.*—Owing to the very viscous nature of the concentrated solutions it was impossible to get points on the curve beyond those shown, and no acid salt was isolated, the solid phase being the acid in every case. The compositions shown are those of the solution.

Rubidium (—)mandelate.

Acid, % ...	10·1	10·0	10·5	11·3	13·0	20·7	26·9	34·2	39·0	41·2	45·3	45·8*	45·5
Salt, % ...	0·0	3·1	6·1	8·7	13·7	21·8	27·9	31·4	33·8	34·3	40·8	41·9*	44·9

* Composition of residue : acid, 71·6 ; salt, 20·8%.

6. *The System (—)Mandelic Acid–Cæsium Mandelate–Water.*—The same difficulties were encountered in the investigation of this system as in the previous case, and no acid salt was isolated. The results are expressed similarly.

Cæsium (−)mandelate.

Acid, %	10·1	10·3	11·0	12·0	14·5	25·0	34·9	42·8	44·6	49·4*	49·2†
Salt, %	0·0	2·8	5·0	7·1	11·3	19·0	24·3	30·3	32·3	39·4*	42·0†

* Residue: acid, 77·2; salt, 19·3%. † Residue: acid, 69·0; salt, 23·1%.

7. *The System (−)Mandelic Acid–Thallous Mandelate–Water.*—Some of the solutions for analysis were made by mixing appropriate quantities of mandelic acid and thallous carbonate, but later, the crystalline thallous mandelate was used. The composition of the solid phase was determined by the residue method. Some difficulty was experienced at first at high concentrations owing to the separation of two liquid phases. After a few days, however, the lower layer crystallised, and no further trouble was encountered.

Thallous (−)mandelate.

Solution.		Residue.			Solution.		Residue.		
Acid, %.	Salt, %.	Acid, %.	Salt, %.	Solid phase.	Acid, %.	Salt, %.	Acid, %.	Salt, %.	Solid phase.
10·1	0·0	—	—	Acid	18·3*	14·6	24·2	40·2	1 : 1-Acid salt
10·4	2·4	—	—	,,	17·6*	14·6	23·0	33·2	,,
11·2	4·6	—	—	,,	11·3	14·7	—	—	,,
11·4	6·5	—	—	,,	10·0	13·7	17·3	34·2	,,
12·9	9·0	—	—	,,	8·7	13·7	19·4	39·9	,,
15·3	13·7	—	—	,,	7·4	14·1	—	—	,,
16·3	14·3	—	—	,,	5·9	16·2	15·9	36·6	,,
17·8*	16·7	—	—	,,	5·2	17·8	26·3	61·1	,,
19·7*	19·0	—	—	,,	4·5	18·1	15·8	40·6	,,
21·2*	20·8	51·6	14·6	,,	3·1	36·4	17·3	54·6	,,
23·0*	22·0	—	—	,,	3·2	43·7	17·6	57·9	,,
26·3*	27·8	46·3	20·5	,,	3·8	52·2	20·6	62·1	,,
29·2*	28·8	44·6	22·4	,,	5·2	60·1	—	—	,,
19·4	17·0	30·1	21·3	Acid + 1 : 1-salt					

* Metastable points.

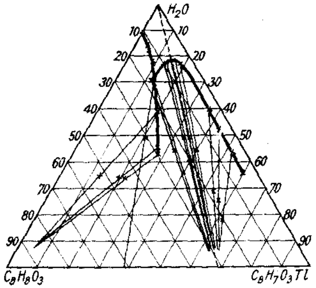
8. *The System (−)Mandelic Acid–Magnesium Mandelate–Water.*—Owing to the slowness with which the systems attained equilibrium, it was necessary to stir them for much longer than usual (40—60 hours). The solubility of the normal salt was found to be 6·08 g. per 100 g. of solution; McKenzie (J., 1899, **75**, 969) found 4·5 g. at 16°, and Findlay and Campbell (J., 1930, 2721) reported 1·96 g. at 25°. In order to confirm the value obtained above, magnesium (−)mandelate was also prepared from equivalent solutions of the ammonium salt and magnesium chloride, being precipitated on boiling. Considerable difficulty was encountered in attempts to determine accurately the composition of the acid salt, because (*a*) the curve is situated almost wholly near the apex of the triangle, and any analytical error is considerably magnified when Schreinemakers's method is applied, (*b*) equilibrium in all systems with magnesium salts is attained very slowly, (*c*) metastable points are found extending into the region where the acid salt is formed. Tie lines coming from the points of intersection of the curve gave solids with 25% and 9·5% of acid in their composition. The acid salt must, therefore, have a composition between these two values. Solids with 18% and 21% acid were obtained from points on the acid salt part of the curve. It appeared likely that the composition of the acid salt for the active mandelic acid was similar to that found for the inactive acid. Solutions of composition corresponding to the centre of the acid salt curve were therefore stirred for 2—3 days with a solid of composition corresponding to this acid salt, and the percentage of acid in the solid did not vary to any considerable extent. Hence, we conclude that the composition of the acid salt in the case of the active acid is almost certainly the same as in that of the inactive acid (17·9% of acid).

Magnesium (−)mandelate.

Solution.			Solution.			Solution.			Solution.		
Acid, %.	Salt, %.	Solid phase.	Acid, %.	Salt, %.	Solid phase.	Acid, %.	Salt, %.	Solid phase.	Acid, %.	Salt, %.	Solid phase.
10·1	0·0	Acid	10·3	4·1	Acid	10·3	4·1	Acid salt	9·9*	6·1	Normal salt
10·0	0·8	,,	10·4*	4·3	,,	10·0	4·2	,,	8·2	5·9	,,
10·1	2·7	,,	10·7*	5·1	,,	9·1	4·4	,,	5·6	5·8	,,
10·4	3·2	,,				8·3	5·6	,,	2·9	5·9	,,
									0·0	6·1	,,

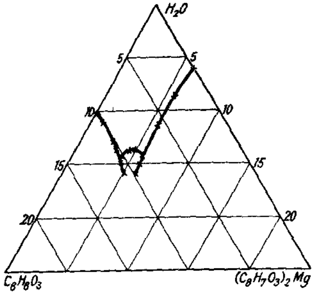
* Metastable points.

FIG. 5.
Thallous mandelate.



Acid salt stable.

FIG. 6.
Magnesium mandelate.



Acid salt unstable.

9. *The System (–)Mandelic Acid–Calcium Mandelate–Water.*—The 1 : 1-salt and the 2 : 1-salt were prepared by crystallising the salt from solutions of (–)mandelic acid. Some difficulty was experienced in freeing the 1 : 1-salt from the mother-liquor and this accounts for the higher percentage of acid found on analysis.

Calcium (–)mandelate.

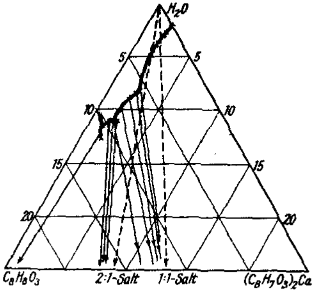
Solution.		Residue.			Solution.		Residue.		
Acid, %.	Salt, %.	Acid, %.	Salt, %.	Solid phase.	Acid, %.	Salt, %.	Acid, %.	Salt, %.	Solid phase.
10·1	0·0	—	—	Acid	8·2	2·1	21·4	18·6	1 : 1-Acid salt
10·2	0·5	—	—	,,	7·5	2·0	45·5	54·5	,,
10·2	1·0	—	—	,,	7·0	2·1	49·3	50·7	,,
10·4	1·1	—	—	,,	6·6	2·1	42·8	57·2	,,
10·9	1·2	—	—	,,	6·1	2·2	—	—	,,
11·2	1·4	42·2	5·4	,,	5·7	2·6	—	—	1 : 1-Salt + normal salt
9·6	1·5	64·3	35·7	2 : 1-Acid salt	4·8	2·3	—	—	Normal salt
9·4	1·8	30·0	16·4	,,	3·8	2·2	—	—	,,
9·1	1·9	27·7	14·8	,,	2·9	2·1	—	—	,,
9·2	1·8	29·8	24·2	2 : 1-Salt + 1 : 1-salt	2·1	2·2	—	—	,,
		...			1·1	2·2	—	—	,,
					0·0	2·3	—	—	,,

10. *The System (–)Mandelic Acid–Strontium Mandelate–Water.*

Strontium (–)mandelate.

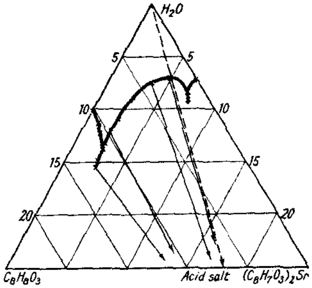
Solution.		Residue.			Solution.		Residue.		
Acid, %.	Salt, %.	Acid, %.	Salt, %.	Solid phase.	Acid, %.	Salt, %.	Acid, %.	Salt, %.	Solid phase.
10·1	0·0	—	—	Acid	6·0	2·9	—	—	Acid salt
10·3	0·9	—	—	,,	4·8	3·2	30·3	69·7	,,
10·4	1·8	—	—	,,	2·0	5·0	8·4	20·8	,,
10·7	2·4	—	—	,,	1·2	6·1	—	—	,,
12·7	2·6	17·0	16·4	Acid salt	1·3	7·4	—	—	,,
11·2	2·5	—	—	,,	1·6	7·7	—	—	,,
9·8	2·6	30·7	69·3	,,	0·8	7·0	—	—	Normal salt
8·4	2·4	—	—	,,	0·0	7·4	—	—	,,
6·4	2·8	—	—	,,					

FIG. 7.
Calcium mandelate.



Both acid salts unstable.

FIG. 8.
Strontium mandelate.



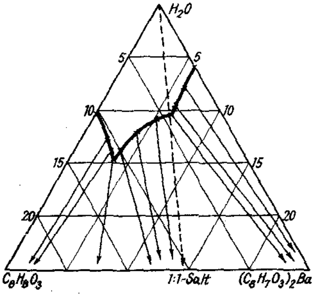
Acid salt stable.

11. *The System (−)Mandelic Acid–Barium Mandelate–Water.*—The residue method was used in the analysis of the solid phase.

Barium (−)mandelate.

Solution.		Residue.			Solution.		Residue.		
Acid, %.	Salt, %.	Acid, %.	Salt, %.	Solid phase.	Acid, %.	Salt, %.	Acid, %.	Salt, %.	Solid phase.
10·1	0·0	—	—	Acid	5·7	5·3	16·0	20·8	Acid salt
10·4	2·3	26·8	1·9	,,	4·1	6·2	10·4	16·3	,,
10·7	3·2	18·6	3·0	,,	4·0	6·3	3·6	15·7	Normal salt
10·9	3·7	26·4	23·0	Acid + acid salt	3·5	6·2	3·6	43·8	,,
10·0	3·7	23·5	33·7	Acid salt	2·0	5·9	1·8	28·3	,,
7·8	4·2	28·1	34·0	,,	0·0	6·0	—	—	,,

FIG. 9.
Barium mandelate.



Acid salt stable.

The analytical data of the various *salts* are tabulated below.

For univalent metals, a 1 : 1 acid salt is of type $C_8H_8O_3,MC_8H_7O_3$. For bivalent metals, the types of acid salt are as follows: 1 : 1 = $2C_8H_8O_3,M(C_8H_7O_3)_2$; 1 : 2 = $C_8H_8O_3,M(C_8H_7O_3)_2$; 2 : 1 = $4C_8H_8O_3,M(C_8H_7O_3)_2$.

Normal salts (anhydrous).

Metal.	Found, %.	Calc., %.
Li	4·3	4·4
Na	13·1	13·2
K	20·4	20·6
Tl^{I}	57·7	57·5
Mg	7·5	7·5
Ca	11·7	11·7
Sr	22·5	22·5

Acid salts (anhydrous).

Metal.	Type of salt.	Found, %. Metal.	Found, %. $C_8H_8O_3$.	Calc., %. Metal.	Calc., %. $C_8H_8O_3$.
Li	1 : 1	2·1	48·8	2·1	49·1
Na	1 : 1	6·8	46·8	7·1	46·6
K	1 : 1	11·2	44·3	11·4	44·4
Tl^{I}	1 : 1	40·3	29·9	40·3	29·95
Ca	1 : 1	—	47·9	—	47·1
,,	2 : 1	4·1	64·1	4·2	64·0
Sr	1 : 2	16·2	28·1	16·2	28·1

Normal salts (hydrated).

	Found, %.		Calc., %.	
	Metal.	H_2O.	Metal.	H_2O.
$Mg(2H_2O)$	6·6	9·5	6·7	9·9
$Ba(\frac{1}{2}H_2O)$	30·6	2·0	30·6	2·0

Acid salt (hydrated), $Ba(C_8H_7O_3)_2,2C_8H_8O_3,\frac{1}{2}H_2O$.

Found, %.			Calc., %.		
Ba.	H_2O.	$C_8H_8O_3$.	Ba.	H_2O.	$C_8H_8O_3$.
18·2	1·3	40·6	18·3	1·2	40·4

No profitable comparison can be made between the inactive and the active mandelates, nor can the effect on the solubility of the acid of the various metal mandelates be studied, until an investigation of the " salting-out " effect of the various metallic ions, now being carried out, has been completed.

SUMMARY.

Solubility curves for the optically active systems (−)mandelic acid–metal mandelates–water at 25° have been investigated in the cases of lithium, sodium, potassium, ammonium, rubidium, cæsium, thallous, magnesium, calcium, strontium, and barium mandelates.

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138. *The Formation and Decomposition of Quaternary Ammonium Salts in Solution.*

By W. CULE DAVIES and R. G. COX.

THE rates of combination of tertiary amines and alkyl halides have been extensively studied in many solvents. The decomposition of ammonium salts in solution, however, has received scant attention. The apparent autoracemisation of solutions of optically active ammonium salts (Pope and Harvey, J., 1901, **79**, 831; Jones, J., 1904, **85**, 229; Wedekind, *Z. Elektrochem.*, 1906, **12**, 330, 515; *Ber.*, 1908, **41**, 1029) was shown by von Halban (*Z. Elektrochem.*, 1907, **13**, 57; *Ber.*, 1908, **41**, 2417; *Z. physikal. Chem.*, 1909, **67**, 129; 1911, **77**, 719; 1913, **84**, 129) to be due to the decomposition of the salt into amine and alkyl halide. Von Halban also showed that other higher ammonium salts, not necessarily having all the groups attached to the nitrogen atom different, decomposed in this way. Velocity coefficients were calculated from the equation for a complete unimolecular change, and, where speeds of formation of such salts were calculated, the equation for a complete bimolecular reaction was used. The coefficients thus obtained often show decided drifts, as would be expected, since equilibria are certainly involved. In the present work the ammonium salt equilibrium in aqueous acetone and in chloroform has been investigated, and rates of formation and decomposition have been calculated by using the appropriate corrected equations. The salts used were the *p*-halogenophenyldimethylallylammonium bromides. Previous determinations of the equilibrium constants of -onium salt equilibria (Essex and Gelormini, *J. Amer. Chem. Soc.*, 1926, **48**, 882, formation of phenyltrimethylammonium iodide in nitrobenzene; Corran, *Trans. Faraday Soc.*, 1927, **23**, 605, decomposition of triethylsulphonium bromide in benzyl alcohol–glycerol mixtures; Williams, Perrin, and Gibson, *Proc. Roy. Soc.*, 1936, *A*, **154**, 684, decomposition of phenylbenzylmethylallylammonium bromide in chloroform) were made at only one initial concentration, and only one direction of the reaction was investigated.

Experimental.

Materials.—Dimethylaniline, purified by treatment with acetic anhydride, was fractionated. *p*-Fluoro- and *p*-chloro-dimethylaniline were prepared from *p*-fluoro- or *p*-chloro-aniline by the following method. A mixture of the substituted aniline (1 mol.), methyl iodide (2 mols.), sodium hydroxide (2 mols.), and methyl alcohol (10 mols.) was heated at 140° for 6 hours in an autoclave. The solvent was expelled, and the residue steam-distilled. The base was warmed with acetic anhydride, and the mixture steam-distilled. *p*-Fluorodimethylaniline, yield 45%, had m. p. 35° (Schiemann and Winkelmüller, *Ber.*, 1933, **66**, 727, gave 25°). *p*-Chlorodimethylaniline, yield 70%, had m. p. 35·5°.

p-Bromodimethylaniline was purified by steam-distillation and recrystallisation from alcohol. *p*-Iododimethylaniline was prepared by slight modification of Weber's method (*Ber.*, 1875, **8**, 715; 1877, **10**, 763).

Commercial allyl bromide was treated with calcium chloride and fractionally distilled; b. p. 69·4—70·0°/747 mm.

The ammonium salts were prepared by warming under reflux for 8 hours at 40° a mixture of the substituted dimethylaniline (10 g.), allyl bromide (30—40 g.), and ether (30 c.c.). The mixture was kept for 12 hours, and the salt filtered off, washed with ether, and recrystallised from alcohol–ether. p-*Fluorophenyldimethylallylammonium bromide* (Found: Br, 30·7. $C_{11}H_{15}NBrF$ requires Br, 30·7%), unlike the following salts, is highly hygroscopic. The p-*chloro*-analogue forms rectangular plates, m. p. 153° (Found: Br, 30·0. $C_{11}H_{15}NClBr$ requires Br, 28·9%), the *p*-bromo-compound rectangular prisms, m. p. 162° (to a red liquid), and the p-*iodo*-compound flat-ended needles, m. p. 150—160° (to a dark red liquid) (Found: Br, 21·8. $C_{11}H_{15}NBrI$ requires Br, 21·7%).

" AnalaR " chloroform was shaken with concentrated sulphuric acid, washed with water, dried over calcium chloride, and fractionally distilled from phosphoric oxide; b. p. 60·5—60·9°/754 mm. It was kept in the dark and gave no indication of the presence of free hydrochloric acid throughout the duration of the experiments.

" AnalaR " acetone, purified by Norris and Prentiss's method (*J. Amer. Chem. Soc.*, 1928, **50**, 3042), and distilled, had b. p. 55·4—56·0°/743 mm.

Densities of Solvents.—Chloroform: $d_{4^\circ}^{14^\circ}$ 1·500; $d_{4^\circ}^{18^\circ}$ 1·492; $d_{4^\circ}^{35^\circ}$ 1·461; $d_{4^\circ}^{45^\circ}$ 1·442; $d_{4^\circ}^{50^\circ}$ 1·433; $d_{4^\circ}^{55^\circ}$ 1·423; $d_{4^\circ}^{60^\circ}$ 1·414; $d_{4^\circ}^{65^\circ}$ 1·404. 5% Aqueous acetone (5 vols. of water made up to 100 vols. with acetone): $d_{4^\circ}^{18^\circ}$ 0·8121; $d_{4^\circ}^{35^\circ}$ 0·7927; $d_{4^\circ}^{55^\circ}$ 0·7696; $d_{4^\circ}^{65^\circ}$ 0·7585. 10% Aqueous acetone: $d_{4^\circ}^{15^\circ}$ 0·8352; $d_{4^\circ}^{18^\circ}$ 0·8280; $d_{4^\circ}^{35^\circ}$ 0·8098; $d_{4^\circ}^{50^\circ}$ 0·7928; $d_{4^\circ}^{55^\circ}$ 0·7868; $d_{4^\circ}^{65^\circ}$ 0·7745. 15% Aqueous acetone: $d_{4^\circ}^{18^\circ}$ 0·8461; $d_{4^\circ}^{55^\circ}$ 0·8030; $d_{4^\circ}^{65^\circ}$ 0·7915.

Velocity Measurements.—Solutions of the base and halide, or of the ammonium salt, were made by diluting weighed amounts to a known volume at room temperature. Knowledge of the density of the solvent at various temperatures then enables the initial concentration to be calculated for any temperature.

Several procedures were adopted in carrying out the reactions. (*a*) *Sealed tube method.* This method was used when the reaction temperature was near or above the b. p. of the solvent, or with very slow reactions. The standard solutions of base and halide were mixed, and known volumes of this mixture, or of the ammonium salt solution, were transferred to test-tubes with constricted necks, which were then immediately sealed. The sealed tubes were placed in the thermostat, the instant of immersion being taken as zero time. At suitable intervals a tube was removed, and its contents washed into light petroleum, which was then repeatedly extracted with water. The aqueous extract was titrated against 0·025*N*-silver nitrate, with potassium chromate as indicator. (*b*) *Reaction vessel method.* The method described by Davies and Lewis (J., 1934, 1599) was used when the reaction temperature was rather below the b. p. of the solvent and when the reaction was fast. (*c*) *Stoppered bottle method.* For very dilute solutions in decomposition experiments, the reaction vessel consisted of a glass bottle with a well-ground glass stopper. Samples were removed by a pipette warmed to the temperature of the reaction and calibrated at that temperature. Greater accuracy was obtained by using one stoppered bottle for each determination in a reaction; in this case a weighed quantity of the salt was added to a known volume of solvent contained in the bottle in the thermostat, and after the desired interval, the contents of the bottle were washed into light petroleum, extraction being done as described above.

Calculations.—(1) For the complete unimolecular reaction $AB \longrightarrow A + B$, $k_1 = 1/t \cdot \log_e a/(a - x)$, where a is the initial concentration of AB at the temperature of the reaction, and x the concentration of A and of B formed after an interval of t minutes (concen-

trations are expressed throughout in g.-mols./l. at the temperature at which the reaction is being investigated). The concentration of AB (ammonium salt) remaining after t minutes is $a - x = y/40 \times v$, where y is the volume (c.c.) of 0·025*N*-silver nitrate required by v c.c. of reaction mixture measured at the temperature of the experiment. In procedure (*a*) the volume of mixture used has to be corrected for change from the temperature of the room to that of the experiment in order to give v, but in procedures (*b*) and (*c*) the volume removed is known directly at the reaction temperature.

(2) For the complete bimolecular reaction $A + B \longrightarrow AB$, with initial concentrations of A and B equivalent and equal to a, $k_2 = x/at(a - x)$, where x is the concentration of AB (ammonium salt) after an interval of t minutes and is equal to $y/40 \times v$.

(3) In reversible uni-bi-molecular reactions, $AB \underset{k_2'}{\overset{k_1'}{\rightleftharpoons}} A + B$,

$$k_1' = \frac{1}{t\,.\sqrt{1 + 4aK}} \log_e \frac{(1 - \sqrt{1 + 4aK})(2Kx + 1 + \sqrt{1 + 4aK})}{(1 + \sqrt{1 + 4aK})(2Kx + 1 - \sqrt{1 + 4aK})}$$

where $K = k_2'/k_1' = (a - n)/n^2$, n being the concentration at equilibrium of A or B, and a and x have the same significance as in (1).

(4) For the opposing reaction in (3),

$$k_2' = \frac{1}{t\,.\sqrt{K'^2 + 4aK'}} \log_e \frac{2a^2 - x[(2a + K') - \sqrt{K'^2 + 4aK'}]}{2a^2 - x[(2a + K') + \sqrt{K'^2 + 4aK'}]}$$

where $K' = k_1'/k_2' = (a - n)^2/n$, n is the concentration of AB at equilibrium, and a and x are as in (2). When the initial concentrations of A and B are unequal, *viz.*, a and b respectively, the following equation holds

$$k_2' = \frac{1}{t\,.\sqrt{(a - b)^2 + K'(K' + 2a + 2b)}} \times \log_e \frac{2ab - x[(a + b + K') - \sqrt{(a - b)^2 + K'(K' + 2a + 2b)}]}{2ab - x[(a + b + K') + \sqrt{(a - b)^2 + K'(K' + 2a + 2b)}]}$$

Generally, k_1' and k_2' were obtained separately by investigating the reaction from both sides, and only in a few cases was the relation $K = k_2'/k_1'$ used to determine a velocity coefficient.

Discussion of Results.

(A) *Aqueous Acetone Solutions.*—The equilibrium position of the reversible reaction between *p*-bromophenyldimethylaniline and allyl bromide lies at *ca.* 50% yield of ammonium salt in 10% aqueous acetone at 50—60°, the same equilibrium being reached from either side. On the assumption that the salt-formation reaction is bimolecular and the reverse reaction is unimolecular, it is possible to obtain values of k_1' and k_2' for the separate reactions by using the equations in (3) and (4). Constant velocity coefficients are obtained throughout the major portion of the reactions. Table I gives an example in detail. The experiments given in Table II show that the assumptions regarding the orders of the reactions used in calculating the separate velocity coefficients are justified. In the salt formation, use of a large excess of either amine or allyl bromide gives good pseudo-unimolecular constants (calculated for a complete reaction), so this reaction is of the second order. The order of the decomposition reaction was found to be unimolecular by isolating it in chloroform solution at or above 55° (see Table V).

Interaction between allyl bromide and aqueous acetone. A simultaneous reaction which might complicate the reactions studied is that between the solvent and the allyl halide. That this reaction is relatively unimportant may be inferred from the fact that the velocity coefficients obtained in both the formation and the decomposition of the ammonium salt are constant throughout the course of the reactions. Further, von Halban and Gast (*Z. physikal. Chem.*, **1916**, **91**, 593) gave the unimolecular velocity coefficient at 65° for the action of 8·7—8·9% aqueous acetone as solvent on allyl bromide (initial concentration 0·78—1·62 g.-mol./l.) as $k_1 = 7 \times 10^{-6}$, which is much lower than the velocity coefficients for the reaction in either direction. However, when the equilibrium mixture of *p*-bromo-

TABLE I.

p-*Bromophenyldimethylallylammonium Bromide.*

Solvent: 10% aqueous acetone. Temp. 65°. (A) Decomposition: $[\text{Salt}]_{65°} = 0{\cdot}09354$. (B) Formation: $[C_6H_4Br{\cdot}NMe_2]_{65°} = [C_3H_5Br]_{65°} = 0{\cdot}09354$. Method (*a*); 5·345 c.c. at 65°.

A. *Decomposition.*

t.	*y.*	*a − x.*	$k_1' \times 10^4$.
90	18·4	0·08606	9·35
120	17·9	0·08373	9·39
180	17·0	0·07950	9·34
245	16·1	0·07530	9·40
300	15·5	0·07249	9·26
360	14·8	0·06923	9·48
460	14·0	0·06548	9·39
485	13·8	0·06455	9·47
∞	11·8	0·05520	—
		Mean $k_1' \times 10^4$ =	9·39

$K^* = 37{\cdot}54$; $k_2'/k_1' = 37{\cdot}27$.

B. *Formation.*

t.	*y.*	*x.*	$100k_2'$.
29	1·7	0·0080	3·46
62	3·3	0·0154	3·53
120	5·3	0·0248	3·44
150	6·3	0·0295	3·60
179	6·85	0·0320	3·48
273	8·5	0·0398	3·50
297	8·9	0·0416	3·58
340	9·3	0·0435	3·50
390	9·7	0·0454	3·45
475	10·3	0·0482	3·47
∞	11·8	0·0552	—
		Mean $100k_2'$ =	3·50

$K'^* = 0{\cdot}02664$.

* K and K' throughout the paper refer to the equilibrium constants calculated from the concentrations of the substances at equilibrium.

TABLE II.

Formation of p-*Bromophenyldimethylallylammonium Bromide.*

Solvent: 10% aqueous acetone. Temp. 65°. Method (*a*); 10 c.c. at 18°.

A. $[C_6H_4Br{\cdot}NMe_2]_{18°} = 1{\cdot}0$; $[C_3H_5Br]_{65°} = 0{\cdot}0468$.

t.	*y.*	*x.*	$100k_1$.
9	3·7	0·00865	2·27
17	6·75	0·0158	2·42
25	9·0	0·0211	2·40
31	10·45	0·0244	2·38
40	12·45	0·0291	2·43
48·5	13·7	0·0320	2·37
55	14·55	0·0340	2·36
65	15·9	0·0372	2·44
		Mean $100k_1$ =	2·38

B. $[C_3H_5Br]_{18°} = 1{\cdot}0$; $[C_6H_4Br{\cdot}NMe_2]_{65°} = 0{\cdot}0468$.

t.	*y.*	*x.*	$100k_1$.
9	4·1	0·00959	2·55
21	8·25	0·0193	2·53
28	10·35	0·0242	2·60
35	11·9	0·0278	2·58
40	13·1	0·0306	2·65
48	14·25	0·0333	2·59
85	17·85	0·0418	2·63
130	20·0	0·0468	—
		Mean $100k_1$ =	2·59

dimethylaniline, allyl bromide, and the ammonium bromide in aqueous acetone is kept for a long time there is a slow increase in the bromide titre corresponding to the above simultaneous reaction. During the times required for attainment of equilibrium, however, the increase in titre is hardly perceptible, so there is usually no difficulty in fixing the values to be taken as the concentrations at equilibrium.

Products of decomposition of an ammonium salt. There are two possible modes of decomposition of *p*-bromophenyldimethylallylammonium bromide, *viz.*,

$$C_6H_4Br{\cdot}NMe_2{\cdot}C_3H_5\}Br \begin{cases} \nearrow C_6H_4Br{\cdot}NMe_2 + C_3H_5Br \\ \searrow C_6H_4Br{\cdot}NMeC_3H_5 + CH_3Br \end{cases}$$

It has been shown that the first of these reactions predominates; for example, 100 c.c. of a solution of the salt ($M/20$) in 10% aqueous acetone were kept in a sealed tube at 65° for 7 days, the acetone then expelled, the residue dissolved in dilute hydrochloric acid, and the mixture neutralised with sodium carbonate. The precipitate, m. p. 54°, mixed m. p. with *p*-bromodimethylaniline, 54·5—55°, weighed 0·327 g. (calc. 0·504 g.). The low yield is mainly accounted for by the difficulty in the separation of the amine after precipitation with sodium carbonate.

Effect of temperature on the ammonium salt equilibrium. Table III summarises the results obtained on the effect of temperature on the formation and decomposition of *p*-chloro- and *p*-bromo-phenyldimethylallylammonium bromide in aqueous acetone, the initial concentration of salt or of amine and allyl bromide being denoted by *a*. The values

of the activation energies are similar to those given in analogous reactions. It will be noted that the substitution of a chlorine for a bromine atom in the *p*-position of the aryl group increases the speed of formation and the yield of ammonium salt, but retards the speed of decomposition of the latter.

TABLE III.

Formation and Decomposition of p-*Chlorophenyldimethylallylammonium Bromide in 10% Aqueous Acetone.*

Temp.	a.	$k_1' \times 10^4$.	$100k_2'$.	K.	Yield of salt at equilm., %.
55°	0·0475	1·94	2·31	111·6	65
65	0·04677	7·19	4·21	58·0	55

$E_1 = 28,920$ cals. $E_2 = 13,250$ cals.

Formation and Decomposition of p-*Bromophenyldimethylallylammonium Bromide in 10% Aqueous Acetone.*

50	0·04747	1·15	1·54	129·7	67
55	0·04709	2·40	2·01	79·68	60
65	0·04677	9·95	3·57	35·92	49

$\log_{10} k_1' \times 10^4 = 21{\cdot}237 - 6842/T$, whence $E_1 = 31,300$ cals.
$\log_{10} k_2' \times 10^2 = 8{\cdot}479 - 2679/T$, whence $E_2 = 12,260$ cals.
$\log_{10} K = 4034/T - 10{\cdot}374$, whence the heat absorbed in the decomposition of the salt or the heat evolved in its formation is $Q_v = 18,450$ cals.

Factors influencing the yield of ammonium salt. The effect of temperature and of initial concentration on the yield of ammonium salt in the formation reaction is given in Tables III and VII. The reversibility of ammonium-salt formation is more common than is generally realised. It is therefore incorrect to heat the mixture of generators, as is often done, with the object of obtaining a good yield of salt. Moreover, the drifts obtained in the bimolecular velocity coefficients (calculated by assuming the formation to be complete) reported by certain workers may be due to the reversibility of the reaction.

Whereas in 10% aqueous acetone at 50° the yield of *p*-bromophenyldimethylallylammonium bromide is 67% (both reactants = $M/20$), in chloroform under the same conditions it is only 1·25%. Increase in the proportion of water in the aqueous acetone has an important effect, augmenting the yield of salt by accelerating its formation and retarding its decomposition (see Table IV). Such effects were predicted by Hughes and Ingold (J., 1935, 244) on the basis of their mechanism for these reactions.

TABLE IV.

Formation and Decomposition of p-*Bromophenyldimethylallylammonium Bromide in Aqueous Acetone.*

Temp.: 65°. Initial concn. of base and halide or of salt at 65° = 0·0467 g.-mol./l.

Solvent.	$k_1' \times 10^4$.	$k_2' \times 10^4$.	K.	Yield of salt at equilibrium, %
5% Aqueous acetone	17·5	127	6·21	19
10% ,, ,,	9·95	357	35·92	49
15% ,, ,,	2·42	562	234·1	74

(B) *Chloroform Solutions.*—The decomposition of $M/20$-*p*-bromophenyldimethylallylammonium bromide in chloroform solution is complete at or above 55°. At 50°, from equivalent quantities of the generators ($M/20$) the yield of salt is 1·25%, and at 35° it is 5%. The decomposition is of the first order, and no correction is necessary for the reverse reaction even at 35° (Table V). The results obtained at an initial salt concentration of approximately $M/20$ for the decomposition reaction are summarised in Table VI.

Change of the nuclear halogen substituent affects the stability of the salt, the order of stability being F>Cl>Br. This should be compared with the order, Cl>Br>I, of decreasing reactivity of the halogenophenyldialkylamines towards alkyl halides (Davies and Lewis, *loc. cit.*). Examination of Table VIII shows that, in spite of the great effect which

TABLE V.

Decomposition of p-*Bromophenyldimethylallylammonium Bromide in Chloroform.*

Initial concn.: 0·04897 at 35°; 0·04739 at 60°. Method (*a*).

35° (10·21 c.c. portions).

t.	y.	$a - x$.	$k_1 \times 10^4$. (1).*	$k_1 \times 10^4$. (2).*
1050	13·2	0·03232	3·96	3·97
1490	11·2	0·02743	3·90	3·92
2640	6·8	0·01665	4·09	4·20
2985	6·0	0·01469	4·03	4·17
4980	2·9	0·00710	3·88	4·30
∞	1·0	0·00245	—	—
		Mean $k_1 \times 10^4$ =	3·97	4·11

* (1) Calculated for the reaction going to completion; (2) corrected for the reverse reaction: K = 1·131.

60° (10·55 c.c. portions).

t.	y.	$a - x$.	$100k_1$.
15	16·6	0·03933	1·24
30	13·7	0·03246	1·26
45	11·3	0·02678	1·27
60	9·4	0·02227	1·26
75	7·6	0·01801	1·29
90	6·4	0·01517	1·27
105	5·4	0·01279	1·25
120	4·4	0·01042	1·26
140	3·4	0·00806	1·27
160	2·6	0·00616	1·28
180	2·0	0·00474	1·28
		Mean $100k_1$ =	1·27

TABLE VI.

Decomposition of p-*Halogenophenyldimethylallylammonium Bromides in Chloroform.**

Temp.	a.	$k_1 \times 10^3$.
p-*Fluoro*-.		
55°	0·04772	2·97
65	0·04697	11·4
E_1 = 29,680 cals.		
p-*Chloro*-.		
55	0·04772	5·87
65	0·04697	24·0
E_1 = 31,090 cals.		

Temp.	a.	$k_1 \times 10^3$.	
p-*Bromo*-.			
35°	0·04897	0·397	
45	0·04832	1·62	
50	0·04801	3·05	
55	0·04758	6·24	Method (*b*)
,,	0·04687	6·25	Method (*a*)
,,	0·04758	6·21 †	
60	0·04739	12·7	
65	0·04786	24·6	

$\log_{10} k_1 \times 10^4 = 20·472 - 6120/T$, whence E_1 = 28,000 cals.

* *p*-Iodophenyldimethylallylammonium bromide was almost insoluble in chloroform, and no measurements could be carried out with it.

† This reaction was carried out in a bottle packed with soda glass.

initial concentration has on the value of the unimolecular velocity coefficient, the *p*-chloro-salt remains slightly more stable than the *p*-bromo-salt in a range of dilution of 20—300 l./g.-mol.

In the decomposition of *p*-bromophenyldimethylallylammonium bromide in chloroform the resulting amine was shown to be *p*-bromodimethylaniline by the following experiment. A solution of 0·4012 g. of the salt in 25 c.c. of chloroform was kept at 55° for 24 hours, and then worked up as for the experiment in aqueous acetone (p. 617). The precipitated *p*-bromodimethylaniline had m. p. 54° (mixed m. p. 54·5°). The amount recovered was 0·238 g. (calc., 0·250 g.).

Formation of p-*bromophenyldimethylallylammonium bromide at* 35° *in chloroform solution.* By working with solutions stronger than $M/20$ it is possible to measure the speed of formation of the salt from its generators. Equation (4) must be used in order to obtain constant velocity coefficients. The mean values are discussed later (see Table IX).

Formation of phenyltrimethylammonium iodide in chloroform. At 45° and with initial concentrations of dimethylaniline and methyl iodide *ca.* $M/10$, good bimolecular velocity coefficients are obtained on the assumption that formation of salt is complete. However, at 65° under similar conditions, the bimolecular coefficients drift seriously, indicating that the reverse reaction is now of considerable importance. Separation of salt prevented a determination of the equilibrium position, but it was determined for less concentrated equivalent solutions:

Temp.	Initial concn.	$k_2 \times 10^3$ (calc. for complete reaction).	% Reaction when salt commenced to separate.
45°	0·0967	3·75	20
65	0·0939	13—5	22
,,	0·0470	Equilm. reached when reaction was *ca.* 7% complete.	No separation.

(C) *Effect of Dilution on Velocity Coefficients and Equilibrium Constants.*—In aqueous acetone, dilution has only a small effect on the velocity coefficients of the formation or dissociation of ammonium salts or on the equilibrium constant (see Table VII), the

TABLE VII.

Formation and Decomposition of p-*Bromophenyldimethylallylammonium Bromide in 10% Aqueous Acetone at 65°.*

Initial concns. Amine.	Allyl bromide.	Salt.	$k_1' \times 10^4$.	$k_2' \times 10^2$.	K.	K'.	Yield of salt at equilm., %.
0·09354	0·09354	0·09354	9·39	3·50	37·54	0·02664	59
0·04677	0·04677	0·04677	9·95	3·57	35·92	0·02784	49
0·02339	0·04677	—	11·5 *	4·15	—	0·02775	55
0·04677	0·02339	—	11·5 *	4·14	—	0·02775	55

* Calculated from K' and k_2'.

Reaction between Equivalent Amounts of Dimethylaniline and Methyl Iodide in 10% Aqueous Acetone at 45°.

Initial concn. of base and halide	0·09620	0·04810	0·02405
$100k_2$	4·29	6·20	6·17

increase of coefficient with dilution being most evident in the formation of phenyltrimethylammonium iodide, a reaction which goes to completion under the conditions given. On the other hand, the values of the velocity coefficients of the decomposition of an ammonium salt in chloroform depend on the initial concentration of the salt, the coefficient increasing markedly with dilution (see Table VIII). When velocity coefficients

TABLE VIII.

Effect of Initial Concentration on the Decomposition of Ammonium Salts in Chloroform Solution.

p-Bromophenyldimethylallylammonium bromide.

Temp. 55°	Initial concn. $\times 10^3$	47·58	23·79	11·90	7·925	6·359	3·179
	$k_1 \times 10^3$	6·24	8·30	12·2	14·3	16·0	18·2
Temp. 65°	Initial concn. $\times 10^3$	47·86	15·65	7·820	3·135		
	$k_1 \times 10^3$	24·6	48·0	67·8	79·4		

p-Chlorophenyldimethylallylammonium bromide.

Temp. 55°	Initial concn. $\times 10^3$	47·58	23·79	11·90	7·925	6·359	3·179
	$k_1 \times 10^3$	5·83	8·10	11·6	13·4	15·3	17·2

are plotted against initial concentration, a straight line is obtained below a concentration of 0·02 g.-mol./l.; *i.e.*, the velocity coefficient is directly proportional to the initial concentration of the salt in very dilute solution. It would appear that in dilute solution the decrease of the speed of decomposition with increase in the initial concentration is due to negative catalysts of concentration proportional to that of the salt. Further, since in a decomposition at any particular initial concentration of salt, the unimolecular velocity coefficients are constant throughout the whole course of the decomposition, it is necessary to postulate that the salt and one of the products of the decomposition act as catalysts. These two catalysts must be of almost identical activity. It seems unlikely that the catalyst is a complex of a reactant or product with the solvent, since the index of catalytic activity, obtained by comparison of velocity coefficients, at 65° is almost identical with that at 55°. From graphs of the results given in Table VIII, values of the velocity coefficients at 55° and 65° at certain dilutions were obtained.

***Decomposition of* p-*Bromophenyldimethylallylammoninm Bromide in Chloroform Solution: Ratios of* k_1 *at Various Dilutions to* k_1 *at* M/60, *and Values of* E.**

Dilution	20	60	120	240	380
55°; k_1/k_1 (M/60)	—	1	1·43	1·73	1·87
65°; ,,	—	1	1·46	1·69	1·80
E, kg.-cals.	28·0	33·4	33·9	32·9	32·6

These values of the activation energies at different initial concentrations of the ammonium salt are of interest. In the most concentrated solution, E is very different from the nearly constant values in the dilute solutions, for which the velocity coefficient is proportional to the initial concentration.

The important part played by complex formation between the solvent and the reactants in determining the mechanism of reactions in solution has been stressed by Moelwyn-Hughes and Sherman (J., 1936, 101). If the reaction $A + B \rightleftharpoons AB$ is considered to proceed through an intermediate stage involving the solvent, or if there is a side reaction in which one of the generators combines with the solvent, then the apparent equilibrium constant $K = [A][B]/[AB]$ would be expected to change in value at different dilutions. This, of course, assumes that an appreciable amount of the solvent–reactant complex is formed at the temperature of the reaction. We were unable to detect the production of chloride ion in solutions of *p*-bromodimethylaniline in chloroform kept for long periods at 35°, but nevertheless there appears to be a possibility of complex formation at this temperature. Our results on the equilibrium constant of the reaction between *p*-bromodimethylaniline and allyl bromide in chloroform at 35° (Table IX) do not lead to an entirely satisfactory conclusion The equilibrium constant increases with dilution, but the velocity coefficients do not alter regularly with dilution. If the value of K' obtained in the most concentrated solution is taken to be the most accurate, values for those velocity coefficients which cannot conveniently be directly determined may be calculated. These are given in parentheses in Table IX, and it will be seen that they compare better with the determined values. Experimental errors in the determination of the equilibrium constant in the dilute solutions are large, but the increase in the constant is slightly too large to be ascribed to this cause. Search is being made for a pair of generators which will give an equilibrium position in chloroform less far displaced towards one side.

TABLE IX.

Initial concn.	$k_1 \times 10^4$.	$k_2' \times 10^4$.	K'.	Amount of salt at equilm., %.
0·1958	3·4 *	6·3	0·541	22
0·0979	5·9 * (4·1)	7·5	0·793	10
0·04897	4·0	4·5 * (7·4)	0·886	5

* Calculated from k_1 or k_2' and K'.

SUMMARY.

1. The formation of certain ammonium salts in solution in aqueous acetone and in chloroform is reversible.

2. The equilibrium constant in aqueous acetone is constant over a range of initial concentrations. In chloroform, however, the equilibrium constant increases with dilution; the effect of complex formation of the participants with the solvent is discussed in this respect.

3. The unimolecular velocity coefficients for the decomposition of ammonium salts in chloroform solution increase with decrease of initial concentration of the salt; in dilute solution the velocity coefficient is proportional to the initial concentration of the salt.

TATEM LABORATORIES, UNIVERSITY COLLEGE, CARDIFF. [*Received, February 9th,* 1937.]

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139. *The Absorption Spectrum of Potassium Cobaltous Thiocyanate.*

By O. RHYS HOWELL and ALBERT JACKSON.

THE general theory has been advanced (Hill and Howell, *Phil. Mag.*, 1924, **48**, 833; see also *Ann. Reports*, 1927, **24**, 288) that the colour of the cobaltous compounds is determined by the number of atoms or groups surrounding the cobalt atom: with six, the colour is red; with four, it is blue.

The transition from red to blue by addition of hydrochloric acid to aqueous cobalt

chloride solution has been followed by measuring the absorption spectra of a series of solutions containing the same amount of cobalt chloride with increasing concentration of hydrochloric acid (Howell and Jackson, *Proc. Roy. Soc.*, 1933, *A*, **142**, 587). It was shown that the state of the cobalt atom was determined by its environment, *i.e.*, by the relative number of chlorine atoms to water molecules in the solution. The curves for the extinction coefficient against the concentration of hydrochloric acid were discontinuous, and at these discontinuities the relative number of chlorine atoms to water molecules formed a simple ratio. It was thus established that the mechanism of the change is as follows:

$$[Co(H_2O)_6]^{\cdot\cdot} \longrightarrow [Co(H_2O)_4Cl_2] \longrightarrow [Co(H_2O)Cl_3]' \longrightarrow [CoCl_4]''$$

For the two principal bands, the extinction coefficient remains constant with further increasing concentration of hydrochloric acid after the formation of the $[CoCl_4]''$ complex is complete. For the two auxiliary bands, however, the value continues to increase, more rapidly and reaching a constant value earlier for one band than for the other. This was attributed to depression of ionisation of the complex acid by increasing concentration of hydrogen ion:

$$[CoCl_4]'' + 2H^{\cdot} \longrightarrow [CoCl_4]H' + H^{\cdot} \longrightarrow [CoCl_4]H_2$$

These conclusions accord with the changes observed in the absorption spectrum of aqueous solutions of cobalt chloride and hydrochloric acid with change of temperature (Howell and Jackson, *Proc. Roy. Soc.*, 1936, *A*, **155**, 33) and also with changes in other physical properties during the transition from red to blue (Howell, J., 1927, 158; 2039, 2843).

The change from red to blue of aqueous cobalt chloride solution on addition of magnesium chloride (Howell and Jackson, J., 1936, 1268) has also been followed spectroscopically as for hydrochloric acid. The curves for magnesium chloride are precisely similar to those for hydrochloric acid, and the mechanism of the change is exactly the same. With magnesium chloride, however, its solubility at ordinary temperature is not great enough to reach the ratio of chlorine atoms to water molecules requisite for complete conversion into the blue $[CoCl_4]''$.

The change in colour from red to blue of aqueous cobalt chloride solution by addition of potassium thiocyanate (due to the formation of potassium cobaltous thiocyanate) has now been examined in a manner exactly analogous to that for the addition of hydrochloric acid or of magnesium chloride. The replacement of water molecules by thiocyanate groups in the complex is determined by their relative numbers in the solution, as is the replacement of water by chlorine, but the course of the change is different in some important particulars.

Many previous investigators have studied the action of potassium thiocyanate on cobalt chloride solution and are agreed that the blue complex $[Co(CNS)_4]''$ is produced, but the stages by which its formation proceeds have not previously been elucidated. Many observations on this colour change, as on those of other cobaltous compounds, are invalid because it has been assumed that the changes occurring in solution are complete with the visual change of colour. It will be seen from the absorption curves now given, however, that a very great concentration of potassium thiocyanate is required to bring about complete transformation, and that, in solutions which appear wholly blue to the eye, the change may be very far from complete.

EXPERIMENTAL.

Solutions.—As in the previous investigations with hydrochloric acid and with magnesium chloride, a concentration of 12 g. of $CoCl_2,6H_2O$ per l. was employed throughout. Kahlbaum's pure salt, free from iron and nickel, was used.

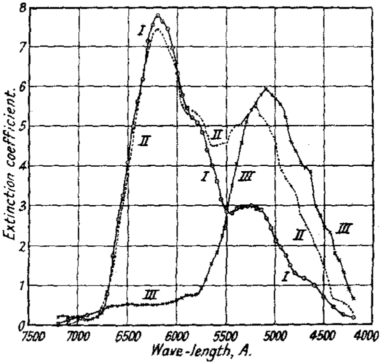
Two stock solutions were prepared, one in pure water and the other in potassium thiocyanate solution containing 960 g. of pure salt per l. A series of intermediate solutions, all containing the same concentration of cobalt but varying amounts of potassium thiocyanate, were prepared by mixing x c.c. of one of the stock solutions and $100-x$ c.c. of the other, both at 18°, and making the mixture up to 100 c.c. with water at 18°. An exactly similar series of solutions was prepared from water and a stock solution of 960 g. of pure thiocyanate only per l., for use as com-

pensating blanks in the other beam. All concentrations were checked by titration against standard silver nitrate solution, iron alum being used as indicator.

Apparatus.—All measurements were made with the Hilger–Nutting spectrophotometer used in the previous investigations. The same accurately ground glass cells were again employed, and were immersed in the special thermostat already described. The working temperature was 20° ± 0·01°, and readings were taken every 50 A. from 7200 to 4200 A.

Results.—The values of the Bunsen extinction coefficient were plotted against the wave-length for each solution. Typical curves for the wholly red (III), a partly blue (II), and a wholly blue solution (I) are given in Fig. 1. It is seen that the curves for the blue form are similar to those obtained with hydrochloric acid and with magnesium chloride, except that they lie further into the region of shorter wave-length and are slightly more extended.

Fig. 1.



I. Concentration of KCNS : 960 g./l. Scale : as shown.
II. Concentration of KCNS : 360 g./l. Scale : × by 0·4.
III. Concentration of KCNS : 0 g./l. Scale : × by 0·04.

With hydrochloric acid and with magnesium chloride there were four bands at 6950, 6660, 6260, and 6100 A. With potassium thiocyanate there are also four. The two principal bands are well defined at 6200 and 5850 A., but the two subsidiary bands at about 5250 and 4700 A. overlap the maximum of the absorption band of the red form and are ill-defined, especially in the only partly blue solutions.

The values of the Bunsen extinction coefficient (ε) at the two principal band maxima have been read from the curves and are given for each concentration of potassium thiocyanate in Table I (*d* is the thickness of the layer). They are plotted against the concentration of potassium thiocyanate in Fig. 2. The subsidiary bands, as already indicated, cannot be read accurately; also, the values of the extinction coefficient are low, so that the experimental error becomes appreciable in comparison with the change occurring with increasing concentration. As previously pointed out, the change in the absorption band of the red form cannot be followed because it is so profoundly affected by the overlapping absorption of the much more intense blue form, for which correction would be excessive.

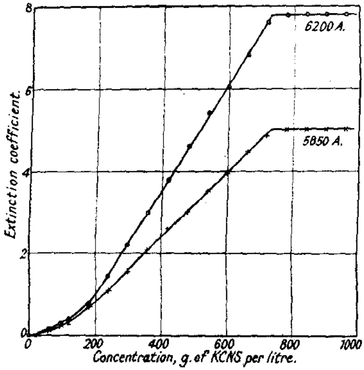
Discussion.

There is one remarkable difference between the curves of the extinction coefficient against concentration for potassium thiocyanate (Fig. 2) and those for hydrochloric acid, in that production of a blue constituent begins at once. The reason for this profound difference will appear below. In other respects the curves for potassium thiocyanate are essentially similar to those for hydrochloric acid. With increasing concentration there is the same

increasingly rapid rise in the extinction coefficient, which merges into a linear relation; this ceases abruptly at a value which remains unchanged with further increasing concentration.

For the addition of hydrochloric acid or of magnesium chloride, the slope of the linear portion of the curve is extremely steep. The concentration at the transition from the curved to the linear relation was therefore obtained without appreciable error by projecting the line to strike the axis of concentration. With potassium thiocyanate, however, the linear portion has a very much more gradual slope. This is due to the fact that, over the linear range, with hydrochloric acid or with magnesium chloride, only one remaining molecule of water is being replaced in the complex (by a chlorine atom), whereas with potassium thiocyanate, as will be shown, three molecules of water are being replaced (by

Fig. 2.



thiocyanate groups). The concentration at which the curve first becomes linear is therefore considerably different from that at which the projection of the linear graph strikes the axis of concentration; moreover, the values for the projections of the linear portions of the curves for the two bands differ appreciably from one another. It is therefore necessary to

Table I.

d, cm.	KCNS, g./l.	ε at 6200 A.	ε at 5850 A.	d, cm.	KCNS, g./l.	ε at 6200 A.	ε at 5850 A.	d, cm.	KCNS, g./l.	ε at 6200 A.	ε at 5850 A.
10·0	0	0·02	0·02	0·5	300	2·19	1·54	0·25	660	6·80	4·44
1·0	60	0·15	0·12	,,	360	2·98	2·06	,,	720	7·60	4·85
,,	96	0·29	0·26	,,	420	3·78	2·58	,,	780	7·75	5·00
,,	120	0·40	0·30	0·25	480	4·60	3·0	,,	840	7·75	5·00
,,	180	0·78	0·70	,,	540	5·40	3·50	,,	900	7·75	5·00
0·5	240	1·43	1·10	,,	600	6·02	3·95	,,	960	7·75	5·00

take directly the concentration at which the curved portion merges into the linear portion. This is found with reasonable accuracy to be 265 g./l. for each curve. The concentration at which the linear relation ceases and the extinction coefficient attains its constant value is very clearly defined at 730 g./l.

The mechanism already postulated to explain the changes occurring on addition of hydrochloric acid or of magnesium chloride to aqueous cobalt chloride solution should also apply to the addition of potassium thiocyanate. The data for the calculation of the numbers of thiocyanate groups and water molecules in solution at the two critical concentrations

are collected in Table II. It follows that at the beginning of the linear relation there is only one thiocyanate group in the complex. Since the compound is blue, there are only four groups altogether, hence its constitution is $[Co(H_2O)_3CNS]^{\cdot}$. At the end of the linear relation, the substitution is complete and there are four thiocyanate groups present, yielding $[Co(CNS)_4]''$.

It has already been pointed out that the mechanism of the initial change on addition of potassium thiocyanate to aqueous cobalt chloride solution is different from that on addition of hydrochloric acid or of magnesium chloride. Now Hantzsch and Shibata (*Z. anorg. Chem.*, 1912, **73**, 309) have shown, from cryoscopic measurements, that in even moderately dilute solution cobalt thiocyanate is only primarily dissociated, yielding the two ions $[Co(CNS)]^{\cdot}$ and CNS'. Evidently, therefore, addition of potassium thiocyanate yields immediately the red complex $[Co(H_2O)_5CNS]^{\cdot}$.

TABLE II.

Critical concns. of KCNS g./l.	*0*	*265*	*730*
Concn. of thiocyanate groups :			
Concn. of CNS, g.-mols./l.	0	2·73	7·52
Concn. of water molecules :			
Wt. of 100 c.c. of solution, g.	100·4	112·7	132·4
,, KCNS present, g.	0	26·5	73·0
,, $CoCl_2$ present, g.	0·65	0·65	0·65
,, H_2O present, g.	99·8	85·5	58·7
Concn. of H_2O, g.-mols./l.	55·4	47·5	32·6
[CNS]/[H_2O]	0	0·0575	0·231
Ratios	0	1	4·02
Ratios of CNS groups in the complexes	*0*	1	4

Continued addition of potassium thiocyanate does not cause replacement of a second molecule of water by a thiocyanate group, giving a red complex similar to that produced on addition of hydrochloric acid or of magnesium chloride. Instead, two further molecules of water are displaced without introduction of thiocyanate groups, yielding the blue complex $[Co(H_2O)_3CNS]^{\cdot}$. Still further addition of potassium thiocyanate (over the linear portion of the curve) causes replacement of the three remaining water molecules by thiocyanate groups, yielding the also blue complex $[Co(CNS)_4]''$. The complete change is therefore as follows :

$$\underset{\text{(Red.)}}{[Co(H_2O)_6]^{\cdot\cdot}} \longrightarrow \underset{\text{(Red.)}}{[Co(H_2O)_5CNS]^{\cdot}} \longrightarrow \underset{\text{(Blue.)}}{[Co(H_2O)_3CNS]^{\cdot}} \longrightarrow \underset{\text{(Blue.)}}{[Co(CNS)_4]''}$$

The results of previous workers are explained by the findings of the present investigation. Rosenheim and Cohn (*Z. anorg. Chem.*, 1901, **27**, 280) from the preparation and properties of double salts, Zawidzki (*Chem. Polski*, 1910, **10**, 49) from the absorption spectra of potassium cobaltous thiocyanate in organic solvents, de Sweemer (*Natuurwetensch. Tijds.*, 1932, **14**, 231; 1933, **15**, 14) from a study of complex metallic thiocyanates, and Hill and Howell (*Phil. Mag.*, 1924, **48**, 833) from a comparison of the absorption spectra of cobalt pigments and solutions, all conclude that the ion $[Co(CNS)_4]''$ is produced. Hantzsch and Shibata show that the absorption spectrum of cobaltous thiocyanate in 60% potassium thiocyanate solution lies between that of the salt in aqueous solution and in organic solvents. The reason is apparent from our curves, since it is seen that at a concentration of 600 g. of thiocyanate per l., the extinction coefficient is only about three-quarters as great as the constant maximum value.

Bassett's theory that the red colour of cobaltous compounds is due to the electron shift of an unshared electron, and the blue colour to that of an electron shared with another atom, is evidently untenable. He is forced to assume (Bassett and Croucher, J., 1930, 1784) that the " non-ionic complex $[Co(H_2O)_4Cl_2]$ would be pale blue "; our investigations on the addition of hydrochloric acid and of magnesium chloride to aqueous cobalt chloride solution prove conclusively that it is red. Similarly, Bassett is forced to postulate that the complex $[Co(H_2O)_3Cl]^{\cdot}$ is red; our previous investigations show that this complex does not exist, and it has now been proved further that the corresponding complex

$[Co(H_2O)_3CNS]^{\cdot}$ is blue. The demonstration of the formation of this positively charged complex also disproves Bassett's dictum that blue cobaltous cations do not exist.

Although the subsidiary bands are incapable of yielding detailed information (see p. 623), it is evident for the band at 5250 A. that there is little or no increase beyond the point at which the extinction coefficient reaches its constant value for the two principal bands, indicating that the potassium cobaltous thiocyanate is completely or very largely unionised when its formation is first complete :

$$[Co(CNS)_4]'' + 2K^{\cdot} \longrightarrow [Co(CNS)_4]K' + K^{\cdot} \longrightarrow [Co(CNS)_4]K_2$$

It may be noted that the absorption of the $[Co(CNS)_4]''$ complex is very much less than that of the $[CoCl_4]''$ complex. The values of the extinction coefficients at the two principal bands are 7·75 and 5·00 for the former as against 22·0 and 21·6 for the latter at the same temperature (20°).

Further, the values at the two principal bands for $[Co(CNS)_4]''$ are very different from one another, but for $[CoCl_4]''$ they are very close; the percentage differences on the lower values are 55% and less than 2% respectively. This suggests a marked difference between the two principal valencies in $[Co(CNS)_4]''$ and great similarity between those in $[CoCl_4]''$; and this is in accordance with the facts now established that in the formation of $[Co(CNS)_4]''$ only one thiocyanate group enters when the complex is red, whereas in the formation of $[CoCl_4]''$ two chlorine atoms enter practically simultaneously.

Summary.

1. The absorption spectra of a series of aqueous solutions containing a fixed amount of cobalt chloride (12 g. $CoCl_2,6H_2O$ per l. as in previous investigations) with increasing concentrations of potassium thiocyanate have been measured at 20° and plotted.

2. The extinction coefficients at the maxima of the two principal bands, 6200 and 5850 A., have been plotted against the concentration of potassium thiocyanate.

3. The curves are essentially similar to those obtained for addition of hydrochloric acid or of magnesium chloride, except in the important particular that the amount of blue constituent increases rapidly from the beginning.

4. The increase becomes linear at 265 g. of thiocyanate per l. and ceases abruptly at 730 g. per l.; thereafter the extinction coefficient remains constant with increasing concentration of potassium thiocyanate.

5. The ratio of the relative numbers of thiocyanate groups to water molecules in solution at these two critical concentrations is 1 : 4. It follows that these are the relative numbers of thiocyanate groups in the complexes at these two stages.

6. In conformity with the facts that a blue constituent is formed immediately on addition of potassium thiocyanate, and that cobaltous thiocyanate is known to be only primarily ionised, the complete change is :

$$\underset{\text{(Red.)}}{[Co(H_2O)_6]^{\cdot\cdot}} \longrightarrow \underset{\text{(Red.)}}{[Co(H_2O)_5CNS]^{\cdot}} \longrightarrow \underset{\text{(Blue.)}}{[Co(H_2O)_3CNS]^{\cdot}} \longrightarrow \underset{\text{(Blue.)}}{[Co(CNS)_4]''}$$

7. The two subsidiary bands overlap the absorption bands of the red form and are not well defined, but their change with concentration indicates that potassium cobaltous thiocyanate is but little ionised when formation of the complex is first complete :

$$[Co(CNS)_4]'' + 2K^{\cdot} \longrightarrow [Co(CNS)_4]K' + K^{\cdot} \longrightarrow [Co(CNS)_4]K_2$$

8. The relative intensities of absorption of the two complexes $[CoCl_4]''$ and $[Co(CNS)_4]''$ at the maxima of the two principal bands are discussed.

The College of Technology, Manchester. [*Received, February 9th*, 1937.]

NOTES.

Preparation of Diphenyl-p-*tolylamine and Phenyldi*-p-*tolylamine.* By RALPH J. B. MARSDEN.

Diphenyl-p-*tolylamine.*—Diphenylamine (8 g.), *p*-iodotoluene (13 g.), potassium carbonate (8 g.), and copper-bronze powder (2 g.) were heated in boiling nitrobenzene (50 c.c.) for 9 hours (cf. Wieland, *Ber.*, 1907, **40**, 4279; "Organic Syntheses," 1928, **8**, 186). The brown viscous residue left after removal of the nitrobenzene by steam distillation was extracted with ether. The oily residue obtained from the dried extract was treated while still hot with boiling alcohol (2 vols.). The crystallised product was filtered off and dissolved in benzene, and the solution dried by partial distillation of the benzene, saturated when cold with hydrogen chloride gas, and kept for 3 hours. After filtration, the benzene was removed, and the residue distilled under reduced pressure; the fraction, b. p. 230—244°/40 mm., crystallised, and after repeated crystallisation from alcohol was obtained in very pale yellowish-white needles (1·5 g.), m. p. 68·75° (corr.) (Found: C, 88·5; H, 6·7; N, 5·1. $C_{19}H_{17}N$ requires C, 88·0; H, 6·6; N, 5·4%).

Phenyldi-p-*tolylamine.*—Di-*p*-tolylamine (10 g.), iodobenzene (10·3 g.), potassium carbonate (7 g.), and copper-bronze powder (2 g.) were heated in boiling nitrobenzene (50 c.c.) for 11 hours, the nitrobenzene removed by steam distillation, and the residue extracted with benzene. After removal of the benzene the product was distilled under reduced pressure; the fraction, b. p. 210—250°/20—40 mm., solidified in orange-yellow crystals (8·5 g.), which were recrystallised once from ethyl acetate and twice from alcohol, giving pale yellow needles (4 g.), m. p. 109° (corr.) (Found: C, 87·6; H, 7·0; N, 5·1. $C_{20}H_{19}N$ requires C, 87·9; H, 7·0; N, 5·1%).

There is a continuous increase in colour on proceeding from the dead white of triphenylamine to the bright pale yellow of tritolylamine with the addition of successive methyl groups.

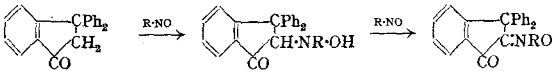
The author thanks Professor N. V. Sidgwick, F.R.S., and Dr. L. E. Sutton for their interest and encouragement, and Imperial Chemical Industries Ltd. for a grant.—THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, March 12th*, 1937.]

Formation of Nitrones by the Action of Aromatic Nitroso-compounds on Methylene Ketones. By ALEXANDER SCHÖNBERG and ROBERT MICHAELIS.

MANY cases have been described of the reaction between 1 : 2-methylene ketones, in alcoholic solution in the presence of alkali or piperidine, and nitrosobenzene (or its derivatives) producing the anils of 1 : 2-diketones (cf., *e.g.*, Skraup and Böhm, *Ber.*, 1926, **59**, 1015):

$$Ph{\cdot}CO{\cdot}CH_2Ph + NMe_2{\cdot}C_6H_4{\cdot}NO \longrightarrow Ph{\cdot}CO{\cdot}CPh{:}N{\cdot}C_6H_4{\cdot}NMe_2$$

It was therefore expected that 3 : 3-diphenyl-1-hydrindone (I) would thus react with nitrosobenzene or *p*-dimethylaminonitrosobenzene to form the 2-anil. The reddish-orange product obtained, however, is not this anil but the corresponding *anil oxide* (III, R = Ph or $C_6H_4{\cdot}NMe_2$). The formation of a nitrone of a 1 : 2-diketone in this way has not hitherto been described, so far as we know. It may be explained by assuming that the primarily formed hydroxylamine derivative (II) is dehydrogenated by nitrosobenzene, somewhat in the same way that the



(I.) (II.) (III.)

hydroxylamine derivative (IV) is dehydrogenated to the nitrone (V) by benzaldehyde in the presence of air (Angeli, Alessandri, and Aiazzi-Mancini, *Atti R. Accad. Lincei*, 1911, **20**, i, 546; Staudinger, *Helv. Chim. Acta*, 1919, **2**, 559).

$$\text{(IV.)}\quad CHPh_2{\cdot}NPh{\cdot}OH \longrightarrow CPh_2{:}NPhO \quad \text{(V.)}$$

The properties of the compounds (III) are in agreement with the suggested formula, *e.g.*, the colour [compare also the colour of (V) and (VIII)]. Their reaction with sulphuric acid, forming 3 : 3-*diphenylindanedione*, is analogous to the formation of benzophenone from the

nitrone (V). The hitherto unexplained formation of the dinitrone (VIII) by the action of diazomethane on nitrosobenzene (Pechmann, *Ber.*, 1897, **30**, 2461, 2870; Staudinger and Miescher, *Helv. Chim. Acta*, 1919, **2**, 560) may be the result of a reaction similar to the formation of (III) from (II). We consider that the diazomethane and nitrosobenzene first produce (VI); this changes to the dimeric form (VII), which then reacts with nitrosobenzene to form the dinitrone (VIII) and phenylhydroxylamine:

$$CH_2N_2 + Ph{\cdot}NO \xrightarrow{-N_2} \underset{\text{(VI.)}}{CH_2{:}NPhO} \longrightarrow \underset{\text{(VII.)}}{[{:}CH{\cdot}NPh{\cdot}OH]_2} \xrightarrow{Ph{\cdot}NO} \underset{\text{(VIII.)}}{[{\cdot}CH{:}NPhO]_2} + NHPh{\cdot}OH$$

The phenylhydroxylamine has not been isolated, but azoxybenzene has been obtained, which is formed from phenylhydroxylamine and nitrosobenzene (Bamberger and Renaud, *Ber.*, 1897, **30**, 2278). In support of the scheme it may be mentioned that diphenyldiazomethane reacts with nitrosobenzene, forming triphenylnitrone, $CPh_2{:}NPhO$ (Staudinger, *Helv. Chim. Acta*, 1919, **2**, 568).

Experimental.

Action of Nitrosobenzene or its p-*Dimethylamino-derivative on* 3 : 3-*Diphenyl*-1-*hydrindone* (I). —1·5 G. of nitrosobenzene (2 mols.) are dissolved in a warm alcoholic solution (70 c.c.) of 2 g. of the ketone, and 0·5 c.c. of 10% aqueous sodium hydroxide added; the solution immediately becomes red. After 24 hours at room temperature, the red crystalline precipitate is filtered off (more may be obtained from the mother-liquor on evaporation), washed with cold alcohol, and recrystallised from absolute alcohol; m. p. 204°. 3 : 3-*Diphenylindanedione*-2-*anil oxide* (III, R = Ph) is sparingly soluble in cold chloroform and warm benzene. It forms an orange-yellow solution in concentrated sulphuric acid (Found: C, 83·3; H, 5·1; N, 3·8. $C_{27}H_{19}O_2N$ requires C, 83·3; H, 4·9; N, 3·6%). An active-hydrogen determination by Zerewitinoff's method gives a negative result.

Under the same conditions, nitrosobenzene being replaced by its *p*-dimethylamino-derivative, 3 : 3-*diphenylindanedione*-2-p-*dimethylaminoanil oxide* (III, R = $C_6H_4{\cdot}NMe_2$) is obtained in deep red crystals, m. p. 233—234°, after recrystallisation from alcohol. A solution in concentrated sulphuric acid is orange-yellow (Found: C, 80·3; H, 5·9; N, 7·0. $C_{29}H_{24}O_2N_2$ requires C, 80·5; H, 5·6; N, 6·5%).

3 : 3-*Diphenylindanedione*.—A mixture of the anil oxide (0·28 g.) or its *p*-dimethylamino-derivative and 45% sulphuric acid (10 c.c.) is rapidly heated to the boiling point, sufficient glacial acetic acid added to dissolve the anil oxide, and the mixture refluxed for 25 minutes. The cooled orange-yellow solution is poured into 100 c.c. of ice-water, and the orange precipitate filtered off and washed with water after 12 hours. After recrystallisation (twice) from ligroin 3 : 3-*diphenylindanedione* has m. p. 152—153°. It is soluble in benzene and easily soluble in pyridine. A solution in concentrated sulphuric acid is yellowish-green (Found: C, 84·3; H, 4·8. $C_{21}H_{14}O_2$ requires C, 84·5; H, 4·7%). The indophenin reaction gives a deep blue-green colour.

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The Transition State in Chemical Reactions.

Opening Contribution to a Discussion on the Transition State in Reaction Kinetics, held by the Chemical Society on February 4th, 1937.

By MICHAEL POLANYI.

IN the time following the announcement of Bohr's theory there was an inclination to think of reactions as " quantum jumps " and to seek the origin of chemical inertia in restrictions which cause certain electronic transitions to be " forbidden." The catalytic decomposition of ozone, for example, was compared with the breakdown of metastable atomic states, such as parhelium, caused by collisions with a wall.

Theory to-day has returned to the older view that chemical reactions consist mainly in a rearrangement of atoms. Take, for example, the decomposition of ozone. A comparison between the arrangement of the atoms of ozone and oxygen in the condensed state shows us that the change consists in a rearrangement of oxygen atoms from one pattern into another (Fig. 1). And the same is true for all chemical reactions : they are not mere changes in electronic states, but generally consist in the breaking up of one molecular grouping and the formation of another in its stead. The causes of chemical inertia must, therefore, be sought in forces which bar the path of atoms trying to break away from old molecules to form new ones. It is the transitions between the old and the new grouping that we will have to consider if we wish to discover the principles of reactivity.

Let us examine the decomposition of ozone into oxygen from this point of view. In ozone we see three bonds linking each molecule, and gaps separating the molecules from one another. In oxygen we have pairs of atoms separated by gaps from other pairs. In both cases the difference between the larger atomic distances, which I have called gaps, and the smaller atomic distances, which correspond to bonds, is well marked. This distinction is characteristic of all definite chemical states.

To rearrange ozone into oxygen, bonds will have to be strained and ultimately severed by gaps. It follows that half-way between ozone and oxygen the distinction between bond-distances and gap-distances will be effaced. This geometrical feature of the transition state can be demonstrated on a pair of ozone molecules decomposing into oxygen. The colliding ozone molecules approach each other to a distance corresponding to the gaps

FIG. 1.

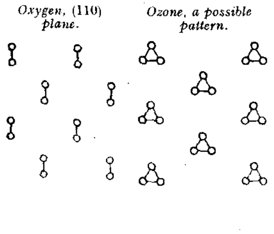
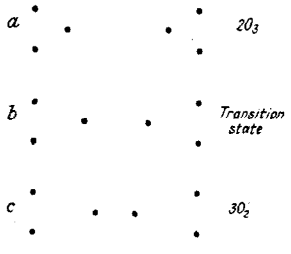


FIG. 2.
Decomposition of ozone (crude picture).



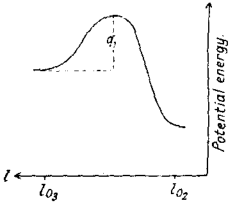
in liquid ozone. Suppose that they are disposed to each other as shown in Fig. 2*a* ; then the decomposition will occur by one atom breaking off from each ozone molecule and joining up to form an oxygen molecule. Fig. 2*c* shows the completed reaction, and Fig. 2*b* the transition state. In this state the separation of the atoms which have gone half-way to form a new oxygen molecule is anomalous and the distances separating these two atoms from the others are also anomalous : they are all larger than normal bonds and smaller than normal gaps.

This transition state can be formed by starting either from a pair of ozone molecules or from three oxygen molecules. In either case we must start by straining the bonds initially present; so from which ever side the transition state is approached, its formation involves expenditure of work. It follows that the reaction on its way through the transition state is accompanied by an initial rise and a subsequent fall of the potential energy; the two chemical states are separated by an energy barrier as shown in Fig. 3. We can now redefine the transition state more precisely by identifying it with the configuration which corresponds to the top of the energy barrier.

The height of the energy barrier q_1 counted from the initial state is the energy required to overcome the chemical inertia. This energy must be present in a collision to make it successful; it is approximately equal to the activation energy measured from the logarithmic temperature coefficient of the velocity constant k_1, *i.e.*, $q_1 = RT^2 . d \log k_1/dT$.

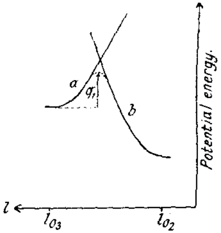
Our ideas of the transition state have acquired precision since London (Sommerfeld Festschrift, Leipzig, 1928; *Z. Elektrochem.*, 1929, **35**, 552) showed that the energy of a system composed of three or four univalent atoms can be defined for any configuration if the bonds which each separate pair of atoms can form with one another are fully known. London's method has been used for calculations of the energy and configuration of the

FIG. 3.



l is the distance between the two oxygen atoms which change their position in Fig. 2. All reactions have such a "reaction co-ordinate" l, which describes the reaction path. The symbol l is used later in this general sense.

FIG. 4.



Curve a = energy of 4 strained ozone bonds.
Curve b = energy of 1 strained oxygen bond.

transition state by Eyring and Polanyi (*Z. physikal. Chem.*, 1931, *B*, **12**, 279), but, although the results have proved illuminating in a general way, their value is restricted by the fact that it is difficult to judge the errors caused by the mathematical approximation involved in the theory.

Fortunately, it is possible in many cases to calculate the energy and configuration of the transition state by means of another method, which is based on very simple assumptions. This method, suggested by Ogg and Polanyi (*Trans. Faraday Soc.*, **1935**, **31**, 604), is applicable to reactions in which ions are formed or which are accompanied by other fundamental changes in electronic structure (Evans and Polanyi, *ibid.*, **1936**, **32**, 1333) such as, *e.g.*, the change of bivalent into quadrivalent carbon.

The method can be demonstrated for the decomposition of ozone (without prejudice to the question whether it is truly applicable in this particular case) as follows: Starting from two ozone molecules in the configuration in Fig. 2*a*, we imagine the two oxygen atoms which lie on the horizontal axis displaced symmetrically in the direction of their position in Fig. 2*c*. We plot the consequent rise in energy while assuming that there is ***no interaction between the two oxygen atoms***, and thus obtain the energy curve of the four strained ozone bonds (Fig. 4, curve *a*). Next, we start from the other side of the reaction, that is, from three oxygen molecules situated as in Fig. 2*c*, and pull the above two oxygen atoms apart towards their position in Fig. 2*a*. We again plot the rising energy, which will be merely

that of a strained oxygen molecule if we *disregard all interaction between the two displaced atoms and the pair of oxygen molecules* flanking them on both sides. Thus we obtain curve *b* in Fig. 4. The reaction will occur at the point where the two curves cross; hence the energy and configuration at the crossing point can be identified with that of the transition state. It is true that, strictly speaking, the energy of the transition state is always lower than that given by the crossing point, since, on account of the quantum-mechanical "degeneracy" of this state the crossing point is cut off as shown by the dotted line in the diagram. An exact calculation of the "perturbation energy" which causes this depression would lead to the same solution as that proposed by London. The perturbation energy, however, is small, and can be neglected in reactions involving a fundamental rearrangement of the electrons; herein lies the practical justification of the method.

However, the main value of this treatment of chemical mechanism does not, perhaps, lie at present in its power to predict activation energies, but rather in the fact that it gives a clear picture of the transition state which leads to an understanding of various *regularities of reactivity and, in particular, to a theoretical parallelism between variations* of velocity constants and equilibrium constants.

Considering an equilibrium between ozone and oxygen, we would see the atoms passing back and forth between the configurations of Fig. 2*a* and *c*, passing on each occasion through the transition state, Fig. 2*b*. The transition state, which we will now call τ, thus takes part in the equilibrium, and we can apply to the "population" of τ (*i.e.*, the number of systems per unit volume which have configurations represented by τ) the fundamental considerations of statistics:

$$\text{Population } (\tau) = \text{birth-rate } (\tau) \times \text{average life } (\tau).$$

Now τ is formed either when a pair of ozone molecules decompose, *i.e.*, "reaction 1" occurs, or when ozone is formed from oxygen by the converse "reaction 2." Birth-rate (τ) is, therefore, the sum of reactions 1 and 2 per unit of time. At equilibrium the numbers of reactions 1 and 2 are equal, and hence

$$\text{reaction rate } 1 = \tfrac{1}{2}\frac{\text{population } (\tau)}{\text{average life } (\tau)}$$

Since τ corresponds only to a single point on the co-ordinate l, the population and average life of τ are both infinitesimal quantities. Pelzer and Wigner (*Z. physikal. Chem.*, 1932, *B*, 15, 445), who first suggested such a statistical discussion of the transition state in a theory of the reaction $H + H_2^{para} = H_2 + H$, have shown that

$$\text{population } (\tau) = c'c''e^{-q_1/RT}\phi_1 \, . \, dl$$

where c' and c'' are the concentrations of the two reactants, q_1 is the activation energy, and ϕ_1 a probability factor which can be determined from the configuration and the elastic properties of the transition state. Wigner also pointed out that the average life (τ) is simply a thermal velocity divided by the infinitesimal length dl, *i.e.*, average life (τ) = v/dl. The velocity constant k_1 was thus obtained:

$$k_1 = \tfrac{1}{2}e^{-q_1/RT}\phi_1 v \quad \ldots\ldots\ldots \quad (1)$$

The novel feature of this expression is the appearance of $\frac{1}{2}\phi_1 v$ as a temperature-independent factor, *i.e.*, representing encounter number × steric factor. This is here derived from the configuration and elastic properties of the transition state. This magnitude, which we will briefly call the "collision factor," was calculated by Pelzer and Wigner (*loc. cit.*) for the reaction $H + H_2^{para} = H_2 + H$. Later, the factor ϕ_1 was given its general form by Eyring (*J. Chem. Physics*, 1935, **3**, 107) and by Evans and Polanyi (*Trans. Faraday Soc.*, 1935, **31**, 875). Eyring (*J. Amer. Chem. Soc.*, 1935, **57**, 985) used it successfully to calculate the collision factor for $2NO + O_2 = 2NO_2$.

More general conclusions can be obtained by introducing thermodynamic variables into equation (1). We define (Evans and Polanyi, *loc. cit.*; Wynne-Jones and Eyring, *J. Chem. Physics*, 1935, **3**, 492, suggest a similar expression) an infinitesimal equilibrium constant

$K_1 . dl$ which determines the population (τ) as a function of the concentrations c' and c'' of the reactants, *viz.*,

$$\text{population } (\tau) = c'c''K_1 . dl$$

and, by the same process as that leading to (1), obtain

$$k_1 = \tfrac{1}{2}K_1 v \quad . \quad . \quad . \quad . \quad (2)$$

Further, we define the free-energy difference F_1 and entropy difference S_1 by

$$\left.\begin{aligned} RT \log K_1 &= F_1 \\ \text{and} \quad F_1 &= -q_1 + TS_1 \end{aligned}\right\} \quad . \quad . \quad . \quad . \quad (3)$$

Starting from the opposite direction of the reaction, we have analogous magnitudes K_2, F_2, S_2, and q_2.

The collision factor $\tfrac{1}{2}\phi_1 v$ now assumes the form

$$\text{collision factor} = \tfrac{1}{2}e^{S_1/R}v \quad . \quad . \quad . \quad . \quad (4)$$

We also note that the thermal velocity v can only change slightly at constant temperature, and we therefore set for any isothermic variable χ

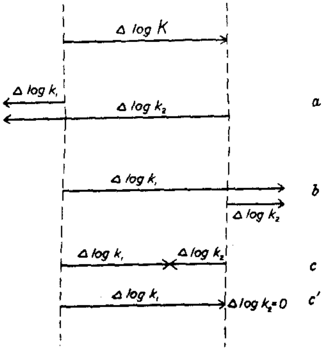
$$\partial v/\partial \chi = 0 \quad . \quad . \quad . \quad . \quad (5)$$

and from (2), (3), and (5) we deduce (Evans and Polanyi, *loc. cit.**)

$$\partial F_1/\partial \chi = RT . \partial \log K_1/\partial \chi = RT . \partial \log k_1/\partial \chi \quad . \quad . \quad . \quad . \quad (6)$$

Before we proceed to apply this equation, we wish to call attention to the fact that the statistical discussion of the transition state implies a further revision of our ideas concerning its nature. The postulate that the transition state is only formed when a reaction occurs in either the forward or the backward direction implies that this state is the point of the reaction path having a minimum statistical probability. This point may not exactly coincide with the maximum of potential energy but corresponds to the maximum of the free energy.

FIG. 5.



A change in equilibrium constant $\Delta \log K$ can be made up in three ways by the changes in velocity constant $\Delta \log k_1$ and $\Delta \log k_2$. A similar classification holds for changes in heat $\Delta Q = \Delta q_1 - \Delta q_2$ and changes in entropy $\Delta S = \Delta S_1 - \Delta S_2$. The case c (and c') is of particular significance.

The purpose of introducing thermodynamic variables relating to the transition state is to deal more easily with relationships between changes in equilibrium and changes in reaction rate. An equilibrium constant K is defined by the reaction velocity constants

$$\log K = \log k_1 - \log k_2$$

When K varies from one reaction to another, *e.g.*, under the influence of chemical substitution, or by a change of solvent, or else by a continuous factor such as hydrostatic pressure, then three alternatives are possible which are shown in Fig. 5, $\Delta \log K$ being the logarithmic change in equilibrium constant. The constituent $\Delta \log k_1$ and $\Delta \log k_2$ terms might behave as in *a* or as in *b* or as in *c*. A similar classification is possible for changes in reaction heat $\Delta Q = \Delta q_1 - \Delta q_2$ and in entropy $\Delta S = \Delta S_1 - \Delta S_2$. It has been found that many series of reactions behave according to *c* (or *c'*), which is due, as we shall presently see, to the fact that significant parameters of

* The subsequent section of this paper is taken from the work of these authors.

the transition state have values lying somewhere between those for the initial and the final state of the reaction. The thermodynamic variables of the transition state permit us to define these parameters and to describe simply this interesting class of reaction.

Take, for example, reactions of the type A + B = AB, which might be the union of two atoms to form a molecule, or alternatively, the addition of two complex particles, *e.g.*, $2CPh_3 = (CPh_3)_2$. In both cases the configuration of the transition state might be expected to be intermediate between those of the initial and the final state and to lie close to the final state. The entropy of the transition state will, therefore, vary from one reaction of this type to another almost exactly as the entropy of the over-all reaction. In fact, a theoretical calculation yields

$$S_1 - S = R \,.\, \ln \frac{h\nu}{kT} \frac{h}{(2\pi m^* kT)^{1/2}} \dagger$$

where ν, the frequency of the bond A–B, and m^*, a compound mass, do not vary greatly from one reaction to another. Since, at the same time, S varies a great deal from one reaction to another, it follows that changes in S will be accompanied by almost equal changes in S_1. Such reactions are thus of the type c' with respect to variation of entropy.

The changes in S consist in a *decrease* with *increasing complexity* of A and B. Thus the reaction $2CPh_3 = (CPh_3)_2$ has a much smaller S than the union of two atoms. This obviously arises from the fact that two complex particles have to be linked up in a very particular way which makes AB an improbable state. The decrease in S_1 which accompanies the decrease in S explains the "slow reactions" of Moelwyn-Hughes and Hinshelwood (J., 1932, 230) in which the collision factor $\frac{1}{2}e^{S_1/RT}v$ [see equation (4)] has exceptionally small values. In fact, a number of "slow" reactions (and perhaps all of them) are additions of the type A + B = AB, in which A and B have complex structures.

We can also compare by this method the collision factor in solutions with that in the gas phase. For example, in the reaction $C_2H_4 + H_2 = C_2H_6$, if its entropy in the gas phase is S, then its entropy in solution, S^*, will be $S^* = S + s_{C_2H_4} + s_{H_2} - s_{C_2H_6}$, where $s_{C_2H_4}$, s_{H_2}, and $s_{C_2H_6}$ are the entropies of solution of ethylene, hydrogen, and ethane respectively. On introducing the measured data, *e.g.*, for carbon tetrachloride solution (Horiuti, *Z. Elektrochem.*, 1933, **39**, 22), it follows that S^* is greater than S by about 7·4 entropy units. Applying the same line of reasoning as before, we might assume that $S_1 - S$ is unchanged by the presence of the solvent, and hence that S_1 increases by the amount $S^* - S$. The corresponding change in the collision factor $\frac{1}{2}e^{-S_1/RT}v$ is a 30-fold increase as compared with the gas state. The presence of the solvent can thus increase the *a priori* probability of the reaction, *i.e.*, quite apart from any change in activation energy. The kinetic interpretation of this effect is to be found in the work done by the internal pressure of the solvent which helps the coalescence of two particles into one.

Considering that the formation of the transition state from two reacting molecules is a process similar to an addition A + B = AB, we might generalise this result as follows: The collision factor in solution as compared with the gas phase is determined by the sum $s_A + s_B - s_\tau$, where s_A, s_B, and s_τ are the entropies of solution of the reactants and the transition state respectively. If the sum $s_A + s_B - s_\tau$ has a positive value, as was the case for $s_{C_2H_4}$, s_{H_2}, and $s_{C_2H_6}$, the collision factor in solution will be greater than in the gas phase.‡ This might offer an explanation for numerous cases in which it has been found that the collision factor in solution is higher than the number of collisions which would occur between the reactants if they were present as gases.

In general, the collision factor in solution can be determined by the entropy of solution of the transition state. Attention has been recently drawn to the fact that entropies of solution of one solute in many solvents decrease linearly with the heat of solution; the same relation holds for some series of different solutes in the same solvent. Assuming that the latter relation holds true, at least approximately, for the reacting molecules and the transi-

† This is equivalent to the assumption made by Polanyi and Wigner (*Z. physikal. Chem.*, 1928, *A*, **139**, 439), as pointed out by Evans and Polanyi (*loc. cit.*).

‡ This result has also been obtained in a somewhat different manner by Wynne-Jones and Eyring (*loc. cit.*).

tion state of their reaction, one would expect the collision factor to decrease with decreasing activation energy when a reaction is carried out in different solvents. This feature is, indeed, well marked in the influence of solvents on the rate of formation of quaternary amines from tertiary amines and alkyl halides (see data given by Moelwyn-Hughes and Sherman, J., 1936, 101).

The electrolytic evolution of hydrogen is a reaction in which both equilibrium and reaction rate vary together under the effect of an outside force, namely, polarisation. The relation between these two variations follows Tafel's over-voltage equation, which can be shown to express the fact that the reaction is of the type *c* with respect to log K. Tafel's equation can, accordingly, be deduced by assuming that the strength with which the electric field acts on the transition state lies intermediate between the strengths of its action on the initial and the final state.

Suppose that we consider electrodes at which the rate-determining step in the discharge of hydrogen consists in the transfer of a proton from an oxonium ion to a metal surface where its charge is neutralised by union with an electron, then the free energy F of this process depends on the polarisation ε as does the free energy of the hydrogen electrode: $\partial F/\partial\varepsilon = nA$, where $n = 1$ is the number of electric charges carried by a proton, and A is Faraday's equivalent. Assuming that the effective charge n of the proton in the transition state has a value intermediate between 1 and 0 (which values correspond to the initial and the final state), we obtain

$$\partial F_1/\partial\varepsilon = \alpha nA\,;\ 0 < \alpha < 1$$

which by use of equation (6) immediately leads to Tafel's equation

$$\log i = \alpha nA\varepsilon/RT + \text{const.}$$

if we measure the velocity constant by the intensity of the current.*

Other proton transfers, occurring in acid–base catalysis $AH + B = A^- + {}^+HB$ (A = acid; B = base), can be treated in a similar fashion, resulting in Brønsted's equation, which correlates dissociation constants with velocity constants. On the assumption that the variations of the free energy from one acid to another and from one base to another arise purely from variations in the intensity of the molecule's electric field, the derivation would be exactly the same as that of Tafel's equation. But it seems more appropriate to leave the exact nature of the parameter which causes the variations in the dissociation constants open, and, denoting this unknown parameter by χ, to define another parameter as the derivative of the free energy with respect to χ, denoting it by β, and β_2 for the initial and the final state respectively:

$$\partial F/\partial\chi = \beta_1 - \beta_2$$

Brønsted's equation then results if

$$\partial F_1/\partial\chi = \beta$$

has a value about half-way between β_1 and β_2, *i.e.*,

$$\partial F_1/\partial\chi = \alpha(\beta_1 - \beta_2), \text{ where } \alpha \sim 0{\cdot}5.$$

This gives $\partial F_1/\partial F = \alpha$, and hence, from equations (2) and (3),

$$\log k_1 = \alpha \log K + \text{const.}$$

which is Brønsted's equation if $\alpha \sim 0{\cdot}5$.

Clearly, this framework is appropriate to express also the other numerous cases of logarithmic proportionality between the constants of equilibrium and velocity preliminary to a detailed analysis of the relevant parameters χ and β.

Another promising field for these considerations is the influence of hydrostatic pressure π on reaction rate in solutions. According to van't Hoff, $\partial F/\partial\pi = V_1 - V_2$, V_1 and V_2 being the volumes of molar solutions of the reactants in the initial and the final state.

* This derivation of Tafel's equation becomes identical with the derivation given by Horiuti and Polanyi (*Acta Physicochim. U.S.S.R.*, 1935, **2**, 507) if we assume $F_1 = q_1$, which corresponds to the earlier definition of the transition state as being the maximum of potential energy (see above).

Assuming, as before, that for reactions of the type A + B = AB the configuration of the transition state is intermediate between those of the initial and the final state and nearly the same as that of the latter, we might expect to have

$$\partial F_1/\partial \pi = \alpha(V_1 - V_2)$$

where $0 < \alpha < 1$, and α is near to unity, resulting [equation (6)] in

$$\partial \log k_1/\partial \pi = \alpha(V_1 - V_2)/RT$$

and for the reverse reaction

$$- \partial \log k_2/\partial \pi = (1 - \alpha)(V_1 - V_2)/RT$$

The union of two particles to one molecule being generally accompanied by a reduction in volume, $V_1 - V_2$ should be positive, and hence the association should be accelerated and the dissociation impeded by hydrostatic pressure. The acceleration should be almost but not quite as large as the accompanying shift of the equilibrium, the difference between the two being equal to retardation in the rate of dissociation. This prediction has been fully confirmed by Perrin, Gibson, and Williams (*Proc. Roy. Soc.*, **1936**, *A*, **154**, 684) for the reaction benzylmethylaniline + allyl bromide = phenylbenzylmethylallylammonium bromide. *Thus it appears that the direction in the change in reaction rate caused by* hydrostatic pressure can be predicted for reactions of the type A + B = AB, and the magnitude of the change can also be foretold closely enough from the densities of the initial and the final solutions.

One might try to go one step further by considering all bimolecular reactions as association reactions primarily leading to the fusion of the reacting molecules into a transition state. One might expect, therefore, all bimolecular reactions to be accelerated by pressure. It is true that this is confirmed by experience, so far. Nevertheless, this *consideration can hold strictly, and can be formulated quantitatively, only if* A and B unite to the transition state (AB) without any change in the solvation forces and changes in the density of the solution arising from this cause. Thus, predictions appear to be safe enough so long as no ions are involved in the reaction, but otherwise the theoretical analysis is more complex.

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The Transition State Method in Chemical Kinetics.

*Contribution to a Discussion * on The Transition State in Reaction Kinetics, held by the Chemical Society on February 4th,* 1937.

By C. N. HINSHELWOOD.

THERE *can be no fundamental difference between the results of a kinetic treatment and* those of a thermodynamic treatment. The object of the present contribution is to attempt to show that the transition state method and the kinetic method of treating reaction velocity problems are very much more similar than they might appear at first sight. Neither can be said to stand in opposition to the other. The thermodynamic method frequently has the advantage of a greater formal elegance of its equations and a greater generality. On the other hand, this quality is accompanied by the corresponding defect that the magnitudes operated with are often quite inaccessible to experimental control, and further, that the plausibility of certain assumptions cast in a mathematical form is less easy to assess at its face value than it would be with the corresponding assumptions of the alternative method. The most satisfactory attitude is to be willing to derive all the information possible by the impartial consideration of problems from both points of view. The interpretation of kinetic relations in terms of thermodynamics and vice versa is in any case

* *A few additional remarks are added to what was said in the discussion itself.*

a process worth while for its own sake, and seldom fails to enrich one's understanding of the workings of Nature.

In the following, I shall consider a number of problems from both points of view, and the comments will indicate what I consider to be the relative strengths and limitations of the two methods in various connexions.

The kinetic method is based upon the consideration of the equation, Reaction velocity $= PZe^{-E/RT}$, where Z is the number of encounters between the reactants, E the activation energy, and P a factor expressing the probability that other conditions, such as the orientation of all the molecules concerned, the relative motions of their atoms and electrons, and a favourable disposition of the surrounding solvent molecules, are fulfilled. The simple exponential form of this expression has to be modified if the activation energy resides in a considerable number of degrees of freedom. The extra temperature-variable terms could be included in P, which would then be temperature-dependent : whether or not we do so include them, or whether we replace the exponential by a more complicated expression and call P constant, is a matter of convenience only.*

To calculate Z we must know the collision diameters : the collision diameter is obviously not an absolutely sharply defined magnitude. But there is good sense in taking it as the value derived from viscosity (momentum transfer) experiments, and then enquiring what further conditions must be fulfilled. This is equivalent to assuming that we have a normal size for the transition state. The diameter of the transition complex has to be assumed in making calculations by the thermodynamic method also; and unless we assume it to be normal we do not know what value to assign to it. The diameter difficulty comes equally into both methods.

The transition state method sets out to calculate reaction velocities as follows. The statistical theory of equilibria is employed to calculate the equilibrium constant, K, of a transition complex of the reactants; K is then multiplied by a thermal velocity v and by a numerical factor of the order $\frac{1}{2}$, giving $\frac{1}{2}Kv$ for the rate. K is expressible as a product of partition functions for the activated state divided by a product of partition functions for the reactants, and the whole is multiplied by $e^{-E/RT}$. For v, Eyring uses kT/h.

It is instructive to compare the calculation of a reaction velocity by the two methods in the simplest possible case, and then to see in what manner the difficulties increase as we pass from the simplest to more complex cases. We shall see that they increase in a more or less parallel manner in both.

From the point of view of the kinetic theory, the simplest assumption that we can make is that the activation energy resides in two square terms, and that all the collisions with enough energy lead to reaction. This gives for the rate at unit concentrations

$$\left\{8\pi RT\left(\frac{1}{m_1}+\frac{1}{m_2}\right)\right\}^{\frac{1}{2}}\sigma^2$$

If we wish to make the calculation for more complex cases we must make assumptions about the number of degrees of freedom in which the activation energy resides, and about the orientations, and about the internal phases of the molecular motions, and so on. In general, we do not know what to assume about these, and all that we can do is to investigate whether they appear to change in the right direction when we pass from one example to another.

Turning now to the transition state method, we must write down K. For the transition

* The objection has been made that the kinetic method assumes P to be a constant, whereas the thermodynamic method shows it to be related to an entropy, which, being expressible as the integral of specific-heat terms divided by temperature, may be temperature-variable. This objection amounts to comparing the first approximation of one theory with the second approximation of another. For if the specific-heat terms are of importance, the activation energy will vary with temperature. Variation of activation energy with temperature means that there are different probabilities of reaction for different states within the range of what might be called the spectrum of activated states. In this case the simple exponential form no longer expresses the reaction velocity : or, if it is made to do so formally, then a temperature-variable residuum has to be included in P. This state of affairs has long been familiar in connexion with theories of unimolecular reactions.

complex we shall have a product of three translational partition functions, one rotational (3-dimensional) partition function, and a whole series of vibrational partition functions; for the reactants, we have a product of three translational partition functions for each molecule concerned, a rotational function for each, and a whole series of vibrational ones. In the simplest case, say the union of two atoms to form a molecule, the expression for the K reduces to the form $T_a^3 . R_a/T^6$, where T_a^3 means a product of three translational partition functions for the activated state.

Putting in the values for the different kinds of partition function, and multiplying by kT/h and by $e^{-E/RT}$, we obtain for the rate.

$$\frac{\left\{\frac{2\pi(m_1 + m_2)kT}{h^3}\right\}^{\frac{3}{2}} \cdot \frac{8\pi^2 I kT}{h^2} \cdot \frac{kT}{h}}{\frac{(2\pi m_1 kT)^{\frac{3}{2}}}{h^3} \cdot \frac{(2\pi m_2 kT)^{\frac{3}{2}}}{h^3}} \cdot e^{-E/RT}$$

We must now put in the value for the moment of inertia. If this is written as $\mu\sigma^2$, where σ is the sum of the normal radii of the reactants, then we have made an assumption not very different from that of the simple kinetic theory. If we wish to assume a very different value, then we are doing something which must be equivalent to making the assumption of an abnormal target area in the kinetic theory. In one method as in the other it is difficult to know what value we should take, if for any reason we believe the normal one to be inadmissible. There will be, of course, small differences according to whether we take σ to be the diameter of the product or that of the unchanged pair of reactants, but it is no exaggeration to say that the difference is well within the limits of the other uncertainties. Taking σ as the normal value, we obtain for the rate the expression :

$$(8\pi kT)^{\frac{1}{2}}\left(\frac{m_1 + m_2}{m_1 m_2}\right)^{\frac{3}{2}} . I$$

$$\text{Since } I = \frac{m_1 m_2}{m_1 + m_2} . \sigma^2, \text{ this becomes } \left\{8\pi kT\left(\frac{1}{m_1} + \frac{1}{m_2}\right)\right\}^{\frac{1}{2}} \sigma^2$$

which agrees with that obtained the other way. This is a very neat example of the interrelation of kinetic theory and thermodynamics.

In more complicated cases the partition products do not reduce to the simple form. We obtain products involving a number of vibrational and rotational partition functions for the activated state divided by a similar product for the reactants. The closer study of these products reveals several interesting things. If we are dealing with an association reaction there will be a number of vibrational partition functions for the activated state divided by rotational functions for the reactants. In general, the numerical values of the former are smaller than those of the latter; the result is a small value of K and a correspondingly small reaction rate. This corresponds to a small value of the factor P. The kinetic interpretation of this is clearly that in an association reaction rotational degrees of freedom disappear and new linkages appear with associated vibrations, and that this process can only take place when the mutual orientations of the reactants are suitable, and when the relative motions of various atoms are also suitable for the creation of the new bonds. Each method of statement illuminates the other. As regards the possibility of making quantitative calculations, from the kinetic point of view it is evident at once that to specify the orientations and phases correctly is a very difficult task. To write down the appropriate partition functions may sound formally a matter capable of treatment with greater precision. But this can hardly be true in actual practice. The vibrational partition function depends upon the frequency of the vibration in question, and can easily vary by one or two powers of 10. A product of several can thus vary by many powers of 10. The value of the frequency depends upon the strength of the binding, and precisely in an activated complex, where some bonds are being broken and others formed, we are likely to be very much in the dark as to the appropriate values to take. It is probably not unfair to say that

our chances of writing down the correct values of the partition functions correctly are about the same as those of specifying the orientations and phases correctly.

A point which is relevant here is the question of the identity of the two molecules which constitute the transition complex in a bimolecular reaction. It may be said that the collision theory postulates that their identity is preserved: this, however, is hardly to be insisted on, since we postulate for reaction a state of affairs where the energy exceeds E, where the orientation of the two molecules is between certain limits, and where the phase of their internal motions is also defined. We thus contemplate a structure as specialised as the new species which the thermodynamic method calls the transition state.

In the simplest of cases most of the vibrational degrees of freedom of the reactant molecules might persist more or less unchanged in the transition complex. The corresponding partition functions in the numerator and the denominator of K would cancel. In this case we should be justified in saying that these internal degrees of freedom ought not to be invoked in explaining the reaction rate. But in many cases the activation process must be rather complex: and several, or even many, degrees of freedom in the activated complex possess frequencies very different from those of the normal reactants. If the frequencies are very much smaller, which corresponds to a great loosening of the binding, then the corresponding product of partition functions becomes very great. This corresponds to a large value of P. Here there seems to be no reason why a number of degrees of freedom should not contribute to the activation energy, as in the well-known theories of unimolecular reactions.

These reflexions arise in an interesting way in the question of the effect of solvation on reaction velocity in solution. It has been pointed out that if the transition state is more solvated than the reactants, the temperature-independent factor in the reaction velocity will tend to be small, and vice versa. This follows from considerations of the entropy of activation. The corresponding kinetic statements seem to be as follows. If the activated state is more solvated, it means that the actual reaction process involves the collecting round the reactants of the appropriate number of suitably orientated solvent molecules. The probability of this is small so that P is small. In the converse case we start with solvated reactants: by hypothesis they must become desolvated in the process of activation. From the thermodynamic point of view, the entropy increases when the ordered solvated systems pass into the disordered scattered components with their independent translational and rotational energies. The activation process involves the loosening of the solvated molecules. The frequencies of the links binding them to the reactants become very small in the activated state: this makes the partition function product great, and P great. Kinetically, P is great because the very necessity for loosening the solvate appendages involves the placing of energy in many links; and this, as in the unimolecular reaction theories, causes the expression giving the activation rate to be greater than $Ze^{-E/RT}$ by a large factor.

As I have been invited to contribute to this discussion, I will state my personal view in concluding this section, that the great value of the transition state method is in causing us to think more deeply about the inter-relation of thermodynamic and kinetic magnitudes, rather than in providing us with an essentially more accurate calculus. It must certainly be said that sometimes the answer to a problem may be seen more easily from one point of view than from the other: we can then translate the answer into the language which we prefer.

Another field of usefulness of the transition state method is even more directly thermodynamical. The transition state is regarded as a definite molecular species possessing assignable thermodynamic properties, so that the various thermodynamic relations of common utility can be applied to the equilibrium constant K, enabling one to predict the influence of various factors on rates of reaction.

This leads to many elegant relations, which are formally more satisfying than any which a direct kinetic approach could yield. On the other hand, these relations involve the assignment of values to thermodynamic properties of the transition state, and this is only possible if we know a good deal about the transition state already. In view of the fact that we do not in general know a great deal about the transition state, it is probably best to invert

the obvious procedure, and to use empirical facts about reaction velocity to discover the thermodynamic properties of the transition state. This may lead to valuable generalisations.

One of these may be mentioned as particularly suitable for this method of treatment. Polanyi and Evans, from a study of the influence of pressure on reaction velocity, justify the conclusion that the volume of the transition state is intermediate between that of the reactants and that of the products.

Other cases might be equally simple : some must be less so. For example, we know that the energy of the transition state is not intermediate between that of the reactants and products. When we are thinking of assigning values to thermodynamic properties of the transition state on the basis of analogy with ordinary molecular species, we must remember that the properties of the latter represent averages over the whole of configuration space, while those of the former refer to limited and specialised regions only. Thus it would seem dangerous to apply empirical laws about solubility, or about activity coefficients to the activated state, without special investigations to justify such a procedure. (The fact that the various Brønsted activity coefficient relationships hold is no answer to this demand for caution. The Brønsted relation refers to the influence of Coulomb forces in ionic reactions : nobody would suppose that the total charge on a transition complex is other than the sum of the charges on its constituents.)

To continue the comparison of the two methods, we will now consider a special problem, namely, that of the logarithmic relation between velocity constants of certain series of related reactions.

If we have two series of reactions with velocity constants k_1^a, k_1^b . . . and k_2^a, k_2^b . . . , all members of series 1 and all members of series 2 being chemically analogous among themselves respectively, and the members a, b . . . of a given series differing in the structure of one or other of the reactants or in the substituents present, then we may find a relation of the following form :

$$\log k_1 = \alpha \log k_2 + \text{const.} \qquad (1)$$

where α is the same for all the members of the series a, b . . . . For example, such a relation may be found by plotting the logarithm of the velocity constant for the hydrolysis of benzoic esters with a series of nuclear substituents against $\log k$ for the benzoylation of aromatic amines with the same series of substituents.

Another form which the relation may take is

$$\log k = \alpha \log K + \text{const.}$$

where $\log k$ refers to the velocity constant of a reaction and $\log K$ to the equilibrium constant of another reaction in which one of the reactants can participate. The best known example of this kind is the Brønsted relation between the catalytic coefficient for the action of a series of acids on a given substrate and the dissociation constant in water of the same series of acids.

$\log K$ is proportional to the free energy of the reaction, and $\log k$ can be regarded as proportional to the free energy of the reaction by which the reactants pass to the transition state. If we introduce the thermodynamic equation $d \log k/d\chi = (\beta_1 - \beta_\tau)/RT$ where β is the differential coefficient of the free energy with respect to some variable χ, we can connect the experimental relations referred to above with the thermodynamic properties of the transition state by a simple algebraical elimination.

To account for the linear logarithmic relations we must assume, first, that all the various β's are constants, and secondly, that if the influence of change in structure or substituents is represented by a parameter χ, then the ratio (χ for reaction 1)/(χ for reaction 2) is a constant for all the members a, b . . . of the series. In other words, we translate the experimental relationship into a statement of the kind that certain thermodynamic quantities maintain a constant ratio throughout a series. When we have seen this we have tidied our ideas. The only danger to guard against is the introduction of such a statement as a self-evident truth, which we may be tempted to do simply because we have not enough

intuitive feeling about the quantities in question to see how much assumption such a statement may contain.

Writing the reaction rate in the form

$$\log k = \log PZ - E/RT$$

we may see what the corresponding assumptions of the collision theory must be if equation (1) is to hold. For variations among members of a given series, we have

$$\Delta \log k = \Delta \log PZ - \Delta E/RT.$$

Two cases arise. In the simplest, PZ is constant for a given series, and equation (1) simply requires $\Delta E_1 = \alpha\Delta E_2$. Since PZ often remains nearly constant through a series, this case is of some importance, and is worth examining in more detail. Suppose we are studying the effect of the same series of substituents on two reactions. Let us suppose schematically that one particular bond in each type of molecule is principally influenced by the substituents, their effect on the rest of the molecule being in the first approximation negligible for the purpose of the reaction. If in one case the bond in question is a strong one requiring considerable activation while in the other case it is very weak or requires no activation, we may evidently have ΔE_2 finite but ΔE_1 nearly equal to zero, *i.e.*, $\alpha = 0$. At the other extreme we shall have the bond of approximately equal strength and requiring the same amount of activation in each reaction and $\Delta E_1 = \Delta E_2$ with $\alpha = 1$. In between we shall have fractional values of α. The condition that the fractional value shall be a constant for the series is that the effect of the substituent on the bond strength shall not be an absolute magnitude but one proportional to the original strength of the bond. Alternatively, we may suppose that ΔE_1 is much smaller than ΔE_2 because the effect of the substituent is not wholly transmitted to the part of the molecule where it will influence the activation energy; in this case we must assume, in order to arrive at a constant α, that a constant fraction of the maximum effect is transmitted for all members of the series.

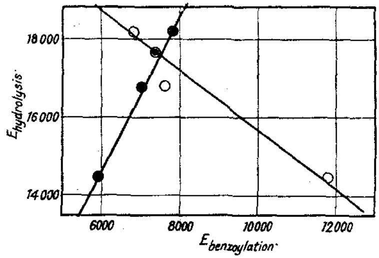
These interpretations are to be compared with the thermodynamic statements made above. They are not in themselves more or less probable than those. They have the disadvantage of being less general, but the advantage of being more easily appraised or verified.

Sub-stituent.	Alkaline hydrolysis of benzoic esters in 85% alcohol. (Ingold and Nathan.)	Benzoylation of nuclear-substituted anilines. (Williams and Hinshelwood.)	Benzoylation of aniline with substituted benzoyl chlorides. (Williams and Hinshelwood.)
Me	18,200	6,800	7800
H	17,700	7,350	7350
NO_2	14,500	11,800	5900
Cl	16,800	7,600	7000

The above table gives the activation energies for three reactions influenced by para-substituents in the benzene nucleus. The figure shows that the variations in activation energy may well be nearly proportional to one another, and that the values of ΔE decrease in the order: substituted amines, esters, substituted acid chlorides. This may well be due to the fact that the transmission of the effect of the substituent is less efficient in the case of the amines than with the esters, while with the acid chloride the effect is produced in a molecule which does not in any case need much activation, most being required in the other reaction partner.

When PZ varies considerably in the series of reactions, the matter is more complicated. In order to preserve relation (1) we most simply assume that $\Delta \log P_1Z_1 = \alpha\Delta \log P_2Z_2$. There are examples where in a series of reactions $\log PZ$ increases linearly with E, so that $\Delta \log P_1Z_1 = \rho_1\Delta E_1$ and $\Delta \log P_2Z_2 = \rho_2\Delta E_2$, and we now have $\rho_1 = \rho_2$ In other words, the at the moment unknown factor which makes PZ increase with E must be one operating equally in the case of both series of reactions. In many cases ρ tends to zero, and it must of course be remembered that the smaller ρ, the less accurately need $\rho_1 = \rho_2$ for relation (1) to be fairly well obeyed. An interesting special case must be mentioned here. At least one example is known in which there are rather irregular, though not very marked, variations in PZ in a series of basic catalyses, and the Brønsted relation is obeyed with great

accuracy. The deviations of *PZ* from constancy seem therefore to be due to a factor which affects the dissociation of an acid and its catalytic power equally. An abnormally great *PZ* for a given acid of the series means that the reaction goes more easily than we should expect from the activation energy. Since the Brønsted relation is obeyed, we infer that that same acid also has an abnormally great tendency to give up a proton to water. If we attribute any anomalous behaviour to that part of the reaction mechanism connected with *the giving up of the proton, rather than to any other kind of activation of the reaction* partner, then we can see how the anomaly may show itself in the *P–E* relation while not



appearing in the Brønsted relation. An examination of various facts from this point of view can provide clues to the nature of *P–E* correlations.

The law connecting the exponential and non-exponential terms of the reaction velocity equation will not be dealt with further here, as it is the subject of another communication from Fairclough and the author (this vol., p. 538).

Nothing has so far been said about the types of reaction to which the transition state method is applicable. It is no criticism of the method itself to mention that it can hardly be applied to chain reactions, or to reactions in which removal of energy from the products is a rate-determining factor. But the wide-spread occurrence of, at least, the former of these two categories shows that special investigation of each given example is necessary.

Study of Transmutation in the Chemical Laboratory.

THE SIXTH LIVERSIDGE LECTURE, DELIVERED BEFORE THE CHEMICAL SOCIETY ON DECEMBER 10TH, 1936.

By F. A. PANETH.

I. *Alchemy.*

I UNDERSTAND that it is laid down in the regulations that every Liversidge Lecture should deal " with the description of new knowledge." I hope that the subject I have chosen will give me the opportunity of complying with this request, although the study of transmutation in the chemical laboratory is by no means new ; if we replace the title by the time-honoured word " alchemy," perhaps it becomes even more obvious that we are in fact speaking of one of the oldest branches of chemistry. An exhaustive treatment of the subject would therefore have to give at least an outline of the history of alchemy, for whatever interests, whether medical, philosophical, mystical, astrological, or even religious, were interwoven with alchemy, its original aim was the transmutation of base into precious metals.

If to-day I intend nevertheless almost completely to neglect past ages, my reason for doing so is by no means lack of interest in, or reverence for, the work of our chemical forefathers. Quite the contrary ; the long history of alchemy is so colourful and fascinating—from the point of view not only of science but also of wider general human culture—that there is a real danger of devoting too much time to the historical part. For we chemists of to-day are more disposed to acknowledge the merits of the alchemists than were our confrères of the 19th century ; their period was in fact the only interval of neglect during the whole 1700 years or so of European alchemy's ascendency. Then many chemists and historians considered alchemy as a more or less interesting form of mental aberration. They overlooked the fact that the growth of metals in the earth—a belief firmly held for centuries by miners and scientists alike—would *a priori* be no more mysterious than the growth of animals or plants ; that there was no known reason why a minute quantity of powder—generally called the " philosopher's stone "—should not transform many times its weight of metal, even as the smallest amount of yeast can raise a large quantity of dough ; and that nothing but the age-long accumulation of an enormous amount of negative experience could reveal the " law of conservation of the chemical elements," just as the failure of innumerable attempts at the construction of *perpetuum mobile* led to the discovery of the " law of conservation of energy."

Even Karl Christoph Schmieder (so far as I know, the only one of the 19th-century historians of alchemy who believed in the reality of some of the reported transmutations) was occasionally too ready to assume fraudulent intentions instead of an earnest desire to investigate. Let me quote just one example of some historical interest in this country. King Henry VI granted to several people a privilege to transmute base metals into gold and silver ; and from the fact that a few years later the cautious Scots decreed by order of Parliament that no British gold should cross the Scottish border, Schmieder concludes that the King's privilege was tantamount to a permit to forge counterfeit coinage. Recently I was interested to find that the original text of the privileges reads quite differently. It states clearly that the King allowed the applicants to experiment on transmutation because he was anxious to find out whether their claims to obtain " perfect gold and silver which could stand all rigid tests " were justified. He expressed his regret that so far " the most learned men had been discouraged from the undertaking by the fear of incurring the penalties under a law made in the reign of our grandfather Henry IV against alchemists " ; he therefore " selected men known to hate all deceitful metallic tinctures " and ordered all his officials to be " favourable and helpful in every way to the performance of this investigation." The documents appear to me to be not in the least discreditable but on the contrary an interesting example of the manner in which an enlightened government tried to promote scientific and industrial research in the 15th century.

The important result emerging from centuries of hard chemical endeavour was the

knowledge that the transmutation of metals was not yet within the reach of men. It was not, however, in a spirit of disappointment that the 19th-century chemists faced this negative result. Most of them entirely abandoned the ideas of alchemy, but found ample compensation in the unexpected achievements of modern chemistry; Liebig probably expressed the general feeling when he declared that chemistry, with its marvellous powers of changing black coal into brilliant colours and efficacious remedies, had taken the place of the philosopher's stone. He and his colleagues were sufficiently far advanced as experimental chemists to see through the alchemists' errors and to be sure that the effects observed with the crude apparatus of previous generations were never due to real changes of one element into another; and to-day, with our knowledge of the extremely narrow limits within which transmutations may occur, we can only confirm their verdict. A glance at an alchemist's laboratory outfit—as shown in many carefully drawn pictures, especially of the Flemish School, in our galleries—is sufficient to convince one that with such primitive gear transmutation could neither be brought about nor detected.

The revival of the idea of alchemy belongs essentially to this century. Two dates are of special importance; in 1896 H. Becquerel detected the invisible rays of uranium, and in 1919 Rutherford and Chadwick observed the emission of a new type of rays when nitrogen was bombarded with α-rays. The former experiment led to the discovery of the spontaneous transmutation of the radioactive substances; the latter was the first example of an artificial transmutation. In the beginning, work on both lines was based on physical methods of detection, with photographic plate, fluorescent screen, electrometer, or Wilson chamber. In the study of the natural radioelements the assistance of chemists was of decisive importance from the very start; it was longer before they could offer any help in the investigation of artificial transmutation. In both cases they applied first radiochemical and later purely chemical methods to the study of the changing elements. It might be best to follow this sequence for to-day's brief record of the new phase in the development of alchemy.

II. *Spontaneous Transmutation.*

It is well known that the discovery of radium in 1898 was due to the new methods of "radiochemistry" introduced by Pierre and Marie Curie. By radiochemistry we understand the application of the methods of chemistry to invisible substances, the effect of the chemical operations being controlled by some sort of apparatus for the measurement of radioactive rays. For example, the barium chloride extracted from pitchblende proved to be active on the electroscope, and each step in the fractional crystallisation showed an increase of activity in the crystals, due to the higher ratio of radium to barium. Finally the new element radium was obtained in visible and weighable quantities.

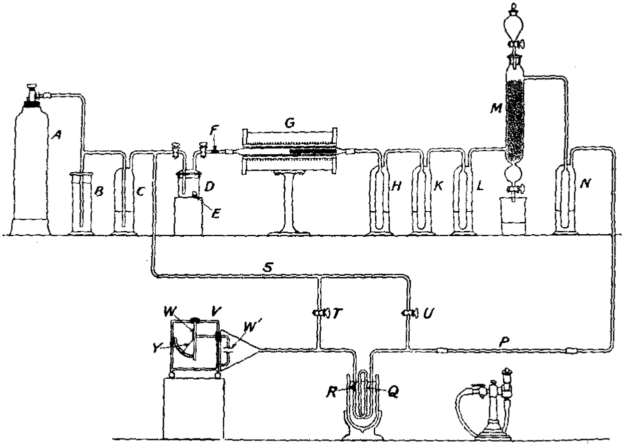
Here radiochemical methods had helped in the discovery of a new element, but not yet in proving the fact of transmutation, as radium was originally present in the material dealt with by Mme. Curie. Exactly the same methods, applied to substances of shorter life, led to the discovery of the fundamental fact that radioactive elements are formed and disappear in our laboratories.

Radiochemical Study of Spontaneous Transmutation.—It will be sufficient to recall here Rutherford and Soddy's experiments on thorium salts in 1902. They detected the possibility of chemically separating from thorium a short-living substance of different character, thorium-*X*; the study of its decay and regeneration gave the clue to the laws governing the radioactive changes. It was known by then that thorium-*X* produces another radioactive substance, of gaseous character; and by a combination of chemical and radioactive methods they were able to demonstrate that this substance, thoron, possesses the nature of a rare gas. This proof, carried out on a quantity of matter probably not exceeding 10^{-14} gram, will always remain one of the outstanding examples of a radiochemical investigation. It can be shown in a simple lecture experiment which illustrates well the general procedure of radiochemistry.

A convenient experimental arrangement is shown in Fig. 1 (taken from my book, "Radioelements as Indicators," New York, 1928, where a detailed description can be found). *E* is a sample of radiothorium. From the steel cylinder *A* a current of nitrogen gas is caused to pass over the radiothorium,

thus carrying the emanating thoron through the cotton wool filter *F* and the different washing bottles, etc., to the electroscope *V*. The discharging effect of the thoron on the electroscope cannot be influenced by any chemical reagent, *e.g.*, hot metallic copper or copper oxide in *G*, oxidising, acid, or alkaline solutions in the washing bottles, or the temperature of a blow-pipe in the quartz tube *P*. From these facts it can be concluded that the gas under examination is of a degree of inertness comparable with that of nitrogen, and possibly even with that of the rare gases. If the nitrogen current is replaced by hydrogen, it is possible to demonstrate the inertness of the radioactive gas under investigation towards red-hot magnesium powder, and thus to prove that it cannot be nitrogen, but must be regarded as a member of the argon group. If the coil *Q* is cooled to the temperature of liquid air, the current of nitrogen immediately loses its power to discharge the electroscope, indicating that the radioactive gas has been removed by this treatment. The correctness of this deduction may be shown by allowing the U-tube containing the active material to warm to room temperature after the condensable product has accumulated for a few minutes. During the warming, the course of the stream of gas is altered, so that the nitrogen no longer passes through *D*, but through *S* and *U* to *V*. The discharge of the electroscope, again seen to take place, clearly demonstrates the fact that the radioactive gas has actually been condensed in *Q* and again vaporised. As the temperature of liquid air suffices for the complete condensation, without any more delicate experiment we can draw the further conclusion that thoron must be one of the heaviest of the group of rare gases.

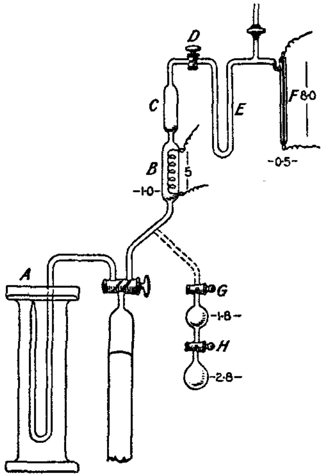
FIG. I.



Radiochemical experiments were not only decisive in establishing the theory of radioactive disintegration; two other important discoveries were also a direct outcome, as Lord Rutherford pointed out a few months ago in his Faraday Lecture to this Society. The impossibility of separating by chemical means substances which in a radioactive sense were distinctly different led directly to the discovery of "isotopes" in the years 1910 to 1913, quite independently of J. J. Thomson's and Aston's studies on positive rays; and the combination of this fundamentally new conception with the genetic relations of the members of the radioactive series enabled Soddy, Russell, and Fajans to formulate the "displacement law." Although nowadays this law seems but a necessary consequence of the theory of atomic structure, and of the origin of α- and β-rays in the nuclei of the radioactive atoms, nevertheless radiochemistry deserves the credit of having discovered in a purely experimental manner this very important law governing natural transformation processes. While places in the periodic table could be assigned to most of the forty or so radioactive substances on the basis of a direct radiochemical study of their properties, the displacement law revealed without any possibility of doubt the positions of those with the shortest life.

Chemical Study of Spontaneous Transmutation.—Although radiochemical methods came into use right at the beginning of the new science of radioactivity, it was not till 1903 that the fact of elementary transformation could be confirmed by classical chemical methods. Here the landmark is Ramsay and Soddy's spectroscopic detection of helium evolved from radium. Although Rutherford's recognition of the α-rays as charged helium atoms naturally led to the expectation that any radioelement which emitted α-rays would develop in the course of time a small amount of helium gas, the possibility of collecting helium in quantity from radium salts was valuable in convincing even the most sceptical that one element had actually been transformed into another. Ramsay and Soddy remarked: "This observation brings ordinary methods to bear on the changes occurring in radioactive bodies," and Rutherford referred to it as the "first definite evidence of the production of a known element during the transformation of radioactive matter."

FIG. 2.



The arrangement of the apparatus for this experiment was very simple—we could still further simplify it to-day—and is shown in Fig. 2, taken from Ramsay and Soddy's paper (*Proc. Roy. Soc.*, 1904, *A*, **73**, 348). The bulb under the stopcock *H* contained a solution of 32 mg. of radium bromide; the evolved electrolytic gas was burnt to water on a red hot spiral contained in *B*, the gases were then dried by phosphoric oxide in *C*, the mercury raised up to *D*, and finally carbon dioxide and radon condensed in *E*. In the spectral tube *F* a brilliant helium spectrum appeared.

Later the production of helium was proved in many of the other substances emitting α-rays. It is not very difficult, provided that radium salts of sufficient strength are available, to prepare also enough radon for a manometric measurement and a spectroscopic investigation. However, these two rare gases are singularly favourable cases, owing to the facility with which they can be separated and spectroscopically identified; besides them, few other products of radioactive disintegration will ever be detected by purely chemical methods. If the half-value period of the new element is long, the amount to be expected might be sufficient, but the radioactive equilibrium is reached too slowly; if, on the other hand, the half-value period is short, the maximum amount will be quickly attained, but then the quantity will not suffice for chemical detection. An example of the former case is the production of ionium from uranium; eventually its quantity will be not less than 1/50,000

of the uranium, but half of this equilibrium amount of ionium will be formed only after 80,000 years. Inversely, if we were to test the production of mesothorium from thorium, seven years would be sufficient to obtain half the maximum amount of mesothorium, but here less than a thousand millionth of the thorium quantity will ever be formed.

Besides helium and radon there is, however, one product of radioactive disintegration whose formation could be chemically detected, owing to its especially fortunate position in the disintegration series. Practically complete decay of radon takes place in one month; and since its immediate disintegration products, radium *A*, *B* and *C*, live only a few hours, after this time practically the whole of the radon is converted into the lead isotope, radium *D*, of a half-value period of 22 years. When in 1914 Dr. Hevesy and myself, working in the Vienna Radium Institute, had one curie of radon at our disposal, we allowed it to decay in a quartz vessel, from the walls of which the radium *D* was dissolved by nitric acid. An electrolysis on a micro-scale produced on a platinum wire anode a yellow coating of radium *D* peroxide; its chemical identity with lead peroxide could be proved by a determination of its electrochemical potential in lead solution.

III. *Artificial Transmutation.*

So far we have dealt only with the radiochemical and chemical detection of the products of spontaneous disintegration. We now proceed to the chemist's share in work on deliberate atomic transmutation.

It was only in the course of things that attempts at artificial transmutation should be made almost immediately after the spontaneous changes of elements had been established, for once it was proved that the atoms of elements were not indestructible it was obviously only a question of finding the right method for performing elementary transmutations at will. It is historically interesting, however, that even much earlier those scientists who believed in a primordial matter, of which all the elements are formed, never gave up the alchemistic conviction that elements can be at least theoretically changed; and I think it especially worth remembering that the very chemist who is usually quoted as the originator of the conception of the chemical element in the modern sense, Robert Boyle, expressed most clearly the doctrine that the stability of chemical elements can only be regarded as relative, since for general philosophical reasons their atoms must be complicated structures. According to him the atoms or, as he calls them, "corpuscles of gold and mercury" are composed of minute particles of the primordial matter, but are "able to concure plentifully to the composition of several very differing bodies, without losing their own nature or texture." Other founders of modern chemistry, *e.g.*, Lavoisier and Dalton, adopted Boyle's chemical views, but had not the deep theoretical insight which enabled him more than 250 years ago to bring the multiplicity of the chemical elements into accord with his belief in the existence of a simple fundamental substance. He had no means of experimentally demonstrating the composite nature of those substances which the strongest reagents of chemical analysis cannot decompose even to-day. But while stating that "corpuscles of a compounded nature may in all the wonted examples of chymists pass for elementary," he always had in mind the possibility that "there may be some agent found out so subtile and so powerfull, at least in respect of those particular compounded corpuscles, as to be able to resolve them into those more simple ones, whereof they consist."

I think there are few examples in the history of the atomistic doctrine which show so clearly the admirable guidance this theory has provided for speculations concerning the nature of matter. Although to-day we do not believe in the existence of a single primordial matter, but speak of four or five particles—neutrons, protons, positrons, electrons and neutrinos—all participating in the structure of the material world, yet Boyle's description of atoms built up of smaller particles, stable in all chemical tests and breaking down only under the influence of an especially potent force, sounds very modern.

The radioelements not only proved by their behaviour that the atoms of elements are changeable, but for the first time placed in our hands an agent of the requisite highly concentrated energy. The first worker who tried to use radioactive rays for artificial transmutations, and was convinced of his success, was William Ramsay. Unfortunately his chemical observations were not controlled by sufficient blank tests and are to be interpreted quite

differently; we now know that any transmutations he may have achieved with the radioactive energy at his disposal were far too small to be detected by his analytical methods, and that all the effects he observed were spurious. As some of his claims were never withdrawn, it may be useful to give in one or two instances the explanation which to-day seems the true one.

Ramsay laid special stress on his experiment showing that in presence of water radon produced not only helium but also neon, a fact which in 1908 he declared to be " indisputably proved." His evidence was faint neon lines in the helium spectrum. Now it can be shown that, owing to the lower excitation potential of neon, a few thousandths of 1% of neon in helium is sufficient to render visible some of the neon lines in the helium spectrum. As Ramsay himself admits that there may have occurred in his experiments an air leakage, shown by the presence of argon, it is fairly obvious that the origin of the neon was that same air leakage. On another occasion, in an old *X*-ray tube, Ramsay discovered helium, which he considered to be a product of the transformation, under the impact of the *X*-rays, either of the elements in the glass walls, or else of the electrodes, or of the gas inside the tube. Suspecting that in this and in many similar cases the presence of helium was nothing but a consequence of the warming of the glass, which makes it pervious to the helium in the atmosphere outside, we made the following simple experiment. We attached a glass tube to an ordinary electric light bulb and let it burn for several days; it was then easy to pump off the gas content and to detect the presence of helium; when, however, the burning lamp was cooled by immersion in water, the amount of helium was too small to be ascertained.

There can be no doubt that all the experiments by Ramsay and his co-workers in which they thought artificial transmutation had been effected are now disproved. However, in fairness to his premature claims, not only should it be emphasised that the radioactive rays which he used in many of his experiments finally led, on an infinitely smaller scale, to success, but one must also make allowance for the much greater difficulties against which he had to contend in his laboratory technique. The presence of air, one of the main sources of error in his experiments, can so easily be avoided by to-day's highly developed vacuum technique that it is well to remember how difficult, or at least tedious, it was to obtain a perfect vacuum in Ramsay's time. I never worked in his laboratory, but having studied micro-gas analysis in Soddy's laboratory in Glasgow in 1913 I am fairly well acquainted with the methods used in those days by Ramsay and his school. I still clearly remember how tiresome it was to evacuate a large glass apparatus by a Töpler pump. After raising the heavy mercury bulb for fifty times or so, one was only too inclined to believe that the vacuum must be absolutely perfect.

The first real success in transmuting elements was obtained by Rutherford and Chadwick in 1919. They also used radioactive rays as the agent " subtile and powerfull," but did not rely on chemical analysis for the detection of the new products, using instead the much more sensitive physical methods for observation of new rays. During the long period from 1919 to 1934 work on artificial transmutation had passed entirely into the hands of the physicists. Not only could chemistry be of no help in these researches, but even radiochemical methods could not be applied. For a capital difference between the natural radioactive substances and the artificially produced elements was that in the radioactive families long series of radioelements follow each other; and, as I stated at the beginning of this lecture, it is very easy radiochemically to control a disintegration process if the product influences an electroscope. But since in the first cases of artificial disintegration by α-rays the products were inactive, there was no possibility whatever of studying their nature by chemical means. In the famous example of the disruption of nitrogen by α-particles,

$$^{14}_{7}N + ^{4}_{2}He \longrightarrow ^{1}_{1}H + ^{17}_{8}O$$

the evidence of the Wilson chamber proved that only two products were formed; hydrogen was identified by its specific charge and mass, and the above equation was thus established beyond reasonable doubt; but no chemical or radiochemical proof could be adduced to identify the new product with an isotope of oxygen.

Radiochemical Study of Artificial Transmutation.—The whole situation changed when in 1923 the artificial radioelements were discovered. Let me mention only one of the first

experiments by I. Curie and F. Joliot. Boron, bombarded with α-particles, yielded an element emitting positrons; its radioactivity decayed with a half-value period of 14 minutes, a time long enough to perform a simple chemical investigation. As a target, boron nitride was used, because boron itself is difficult to dissolve and the presence of nitrogen is of no account in the radioactive observations, since this element is not activated by α-ray bombardment; after irradiation the boron nitride was dissolved in caustic potash, whereby ammonia was produced. It was found that this ammonia carried with it the positron-emitting substance of 14 minutes period; this, of course, was to be anticipated if it were a nitrogen isotope, and so the following mechanism of reaction—which for other reasons was likely to occur—was chemically supported:

$$^{10}_{5}\mathrm{B} + {}^{4}_{2}\mathrm{He} \longrightarrow {}^{1}_{0}n + {}^{13}_{7}\mathrm{N}$$
$$^{13}_{7}\mathrm{N} \longrightarrow {}^{0}_{1}e + {}^{13}_{6}\mathrm{C} \quad (T = 14 \text{ mins.})$$

The complete analogy between this radiochemical proof and those applied since early days in the study of natural radioactivity is, I think, obvious. The only technical difference is that the electroscopes customary for radioactive measurements are rarely sufficiently sensitive for the detection of the weak activities of the artificial radioelements. The instrument mostly used in these investigations is the Geiger–Müller tube connected with some sort of amplifying system. It is not difficult, even in a chemical laboratory, to set up such a simple device—nearly all the apparatus can be bought in any wireless shop—and with its help the chemical nature of very many of the products of artificial transmutation has been studied.

This new field of research became of special interest to chemists when Fermi's discovery of the efficiency of neutrons in producing artificial radioelements showed the possibility of an enormous variety of transmutations. The following two tables give some selected examples to show that one and the same element—ordinary aluminium of mass number 27—can be transformed into various other elements, according to the manner in which it is

TABLE I.

$$^{27}_{13}\mathrm{Al} + {}^{1}_{0}n \longrightarrow {}^{28}_{13}\mathrm{Al}$$
$$^{28}_{13}\mathrm{Al} \longrightarrow {}^{0}_{-1}e + {}^{28}_{14}\mathrm{Si} \quad (T = 2{\cdot}3 \text{ mins.})$$

$$^{27}_{13}\mathrm{Al} + {}^{1}_{0}n \longrightarrow {}^{1}_{1}\mathrm{H} + {}^{27}_{12}\mathrm{Mg}$$
$$^{27}_{12}\mathrm{Mg} \longrightarrow {}^{0}_{-1}e + {}^{27}_{13}\mathrm{Al} \quad (T = 10 \text{ mins.})$$

$$^{27}_{13}\mathrm{Al} + {}^{1}_{0}n \longrightarrow {}^{4}_{2}\mathrm{He} + {}^{24}_{11}\mathrm{Na}$$
$$^{24}_{11}\mathrm{Na} \longrightarrow {}^{0}_{-1}e + {}^{24}_{12}\mathrm{Mg} \quad (T = 15{\cdot}5 \text{ hrs.})$$

$$^{27}_{13}\mathrm{Al} + {}^{1}_{1}\mathrm{H} \longrightarrow {}^{4}_{2}\mathrm{He} + {}^{24}_{12}\mathrm{Mg}$$

$$^{27}_{13}\mathrm{Al} + {}^{2}_{1}\mathrm{H} \longrightarrow {}^{1}_{0}n + {}^{28}_{14}\mathrm{Si}$$

$$^{27}_{13}\mathrm{Al} + {}^{2}_{1}\mathrm{H} \longrightarrow {}^{1}_{1}\mathrm{H} + {}^{28}_{13}\mathrm{Al}$$
$$^{28}_{13}\mathrm{Al} \longrightarrow {}^{0}_{-1}e + {}^{28}_{14}\mathrm{Si} \quad (T = 2{\cdot}3 \text{ mins.})$$

$$^{27}_{13}\mathrm{Al} + {}^{2}_{1}\mathrm{H} \longrightarrow {}^{4}_{2}\mathrm{He} + {}^{25}_{12}\mathrm{Mg}$$

$$^{27}_{13}\mathrm{Al} + {}^{4}_{2}\mathrm{He} \longrightarrow {}^{1}_{0}n + {}^{30}_{15}\mathrm{P}$$
$$^{30}_{15}\mathrm{P} \longrightarrow {}^{0}_{1}e + {}^{30}_{14}\mathrm{Si} \quad (T = 3{\cdot}25 \text{ mins.})$$

$$^{27}_{13}\mathrm{Al} + {}^{4}_{2}\mathrm{He} \longrightarrow {}^{1}_{1}\mathrm{H} + {}^{30}_{14}\mathrm{Si}$$

TABLE II.

$$\left.\begin{array}{l} ^{25}_{12}\mathrm{Mg} + {}^{4}_{2}\mathrm{He} \longrightarrow {}^{1}_{1}\mathrm{H} + {}^{28}_{13}\mathrm{Al} \\ ^{27}_{13}\mathrm{Al} + {}^{2}_{1}\mathrm{H} \longrightarrow {}^{1}_{1}\mathrm{H} + {}^{28}_{13}\mathrm{Al} \\ ^{27}_{13}\mathrm{Al} + {}^{1}_{0}n \longrightarrow {}^{28}_{13}\mathrm{Al} \\ ^{28}_{14}\mathrm{Si} + {}^{1}_{0}n \longrightarrow {}^{1}_{1}\mathrm{H} + {}^{28}_{13}\mathrm{Al} \\ ^{31}_{15}\mathrm{P} + {}^{1}_{0}n \longrightarrow {}^{4}_{2}\mathrm{He} + {}^{28}_{13}\mathrm{Al} \end{array}\right\} \; ^{28}_{13}\mathrm{Al} \longrightarrow {}^{0}_{-1}e + {}^{28}_{14}\mathrm{Si} \quad (T = 2{\cdot}3 \text{ mins.})$$

treated; and that on the other hand one and the same artificial radioelement—radio-aluminium of mass number 28 and half-value period 2·3 mins.—can be produced from very different sources. This recalls in a striking manner the variety of chemical changes effected in molecules by ordinary chemical methods, but this new branch of science deals with the decomposition and synthesis of atomic nuclei, not of molecules. It is alchemy, not chemistry.

As seen from the tables, some of the transformations are effected by bombardment, not

with α-rays or neutrons, but with accelerated particles of hydrogen or deuterium. For these experiments, of course, the high voltage apparatus, or the "cyclotron," of the physicist is necessary, but many of the products have been studied and identified by radiochemical methods. The help of the chemist is, of course, especially welcome in cases where several atomic species are simultaneously formed; for example, he can easily separate, and so distinguish, radioactive sodium from magnesium, if both are produced from aluminium by neutron bombardment.

Chemical Study of Artificial Transmutation.—We have seen that the field of artificial radioelements offers a great number of examples where the success of the transmutation can be checked by radiochemical methods. The last question we have to discuss is whether we are to-day able to study artificial transmutation also by purely chemical means.

It is at once evident that the chemical detection of artificially produced elements will be much more difficult than those of natural transformations. If we have at our disposal a quantity of 100 mc. of radon, then 2×10^{-4} c.c. of helium is formed by its complete decay, and it is quite a simple matter, with our present-day laboratory technique, to identify and measure this amount. If, however, the same quantity of radon is used for the disintegration of nitrogen, in the classical experiment on artificial disintegration mentioned above, the amount of hydrogen produced is only of the order 10^{-9} c.c., as only about 1 in 100,000 α-particles liberates a proton from a nitrogen nucleus. Small as this amount is, it did not seem entirely impossible to detect it chemically; but prolonged attempts in this direction by myself and my co-worker Günther in Königsberg have failed.

It may be useful to compare here the sensitivity of radiophysical, radiochemical, and purely chemical methods in the detection of transmutation. The founder and doyen of the Austrian school of microchemistry, F. Emich, introduced the distinction between "theoretical" and "practical" sensitivity, the former being the smallest amount of a substance which gives an observable effect, the latter the smallest quantity of matter with which an identification can actually be obtained. Here we are concerned only with the practical sensitivity. It is well known that a track in the Wilson chamber, or a kick in the Geiger–Müller counter, is caused by the flight of a single atom, and it may be said, therefore, that the theoretical sensitivity is here one atom. As, however, disintegration follows the laws of probability, a much greater number of atoms of the disintegrating substance must be present if we want to study its rays. The practical sensitivity of the detection in a Wilson chamber or Geiger counter depends in the first place on the half-value period: the shorter this is, the smaller is the quantity of the substance that emits sufficient rays for an identification during the time of observation. On the other hand, too short a period renders the handling of the substance impossible. No systematic investigation has been carried out in order to determine the smallest amount of matter detectable by the above-mentioned physical methods, but we may assume it to be of the order of 10^3 atoms. If the substance has a half-value period comparable with that of radium *C* (20 minutes), at the beginning about one ray would be emitted every 2 seconds and it might be possible to send a sufficient fraction of them into the measuring instrument to enable the substance to be identified. If such a half-value period is long enough for the carrying out of some simple chemical operation, the practical sensitivity of the radiochemical identification can be said to be of the same order of 10^3 atoms.

If the substance is not radioactive, nothing approaching this limit can be obtained. The most sensitive test for an inactive element is, in general, spectroscopic observation; in the case of neon and helium the advantage of a characteristic spectrum is coupled with qualities which make the analytical separation easy. This explains why we could identify pure helium and neon when only some 10^{-10} c.c., or 10^9 to 10^{10} atoms, were present. As already mentioned above, it is possible to detect very small traces of neon in helium; we found that 0·002% of neon can be seen, even if not more than 10^{-7} c.c. of the mixture is available. This means that as little as 2×10^{-12} c.c., or 5×10^7 atoms, of neon can be recognised. Although these are outstanding examples, the practical sensitivity is still 10^4—10^6 times higher than in the radiophysical and radiochemical cases just discussed.

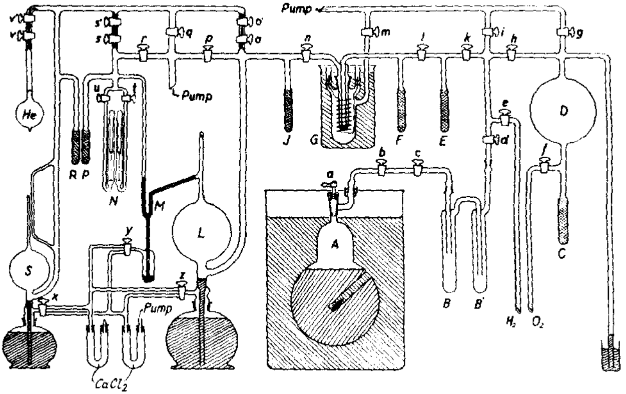
Since the identification limit of helium is especially low, and because several processes of artificial transmutation, all producing helium, are now known, two years ago we renewed

our attempts to prove by purely chemical methods the fact of artificial transmutation. For various reasons we chose the following reaction,

$$^{10}_{5}B + ^{1}_{0}n \longrightarrow ^{4}_{2}He + ^{7}_{3}Li$$

which was discovered by Chadwick and Goldhaber by employing the usual physical methods for the detection of the rays. Our endeavour was to separate the helium from the boron in which it was produced by the neutron bombardment, to purify and to measure it. The last seemed especially interesting, as it is difficult to derive quantitative figures from the physical observations.

FIG. 3.



In Fig. 3 the general arrangement is shown. The copper flask A is filled with boron methoxide; it contains a pocket in which the neutron source, a mixture of beryllium powder and radium (or radon), is placed. As only slow neutrons are captured by boron according to the above equation, the flask A is surrounded by a water tank. We carried out the experiment four times with varying strengths of the neutron source. In the final experiment neutrons produced by the decay of a little more than 2000 mc. of radon, mixed with beryllium, were used for the bombardment of 4 litres of boron methoxide. Less than 10^{-10} gram of boron was disintegrated and the corresponding 10^{-7} c.c. of helium could be separated from the methoxide by boiling the latter. After removal of all the other gases by adsorption on charcoal in the tubes E and F, and the burning of the hydrogen with oxygen in the furnace G, nothing but the small quantity of helium remained. Its purity was tested spectroscopically in the capillary tube on the top of L, and its quantity finally measured by a special manometer N. (Fig. 3 is taken from Proc. Roy. Soc., 1936, A, 157, 417.)

So, by slightly changing Ramsay and Soddy's statement about the first detection of helium in a natural transmutation, we may say that this observation brings ordinary methods to bear on the changes occurring in artificial transmutations. In both cases the qualitative result could be predicted; but the way to quantitative measurements has thereby been opened. And it is evidently a step nearer to the old alchemistic aim, for the whole transmutation can be brought about in the chemist's laboratory without any help whatever from a physicist's apparatus. All we have to do is to prepare radium salt and beryllium metal, mix the two, and bring the mixture near to a boron compound. Then we are sure partly to convert the boron into helium.

If we describe the experiment in such terms, it becomes obvious that some essential features of the procedure of the old alchemists are retained in this process of modern alchemy. However much their descriptions differed in detail they all agreed that the philosopher's stone had first to be prepared; then, directly this miraculous substance was available, by "projecting" it on other substances, these would be transmuted. In our experiment we see the same two steps: first the preparation of the philosopher's stone, the

radium–beryllium tube with its marvellous property of emitting neutrons; and secondly, by the projection of the neutrons on other elements, the transformation of almost any of them. But there is, unfortunately, one serious discrepancy between the alchemists' promises and our achievement. Most of them expected that a small quantity of the philosopher's stone would transmute many times its weight of matter; Louis Figuier in his history of alchemy (1854) has amusingly compared the different claims. Kunckel thought the stone would transmute only twice its own weight, Arnold of Villanova promised 100 times, Roger Bacon 100,000, Isaac of Holland 1,000,000; Raymond Lully thought that each ounce of the transmuted metal would possess the power of transmuting a thousand other ounces, and Salmon even assumed an increase of transmuting power in each such operation. Compared with these claims the modern philosopher's stone is disappointingly feeble. In the radon–beryllium tube about 10,000 α-particles are necessary to produce one neutron, which at its best can transmute only one boron atom into one atom of helium. Hence a big discrepancy between the philosopher's stone and the transmuted matter does exist, and unfortunately on the debit side.

IV. *Future Research on Transmutation by Radiochemical and Chemical Methods.*

As the regulations of the Liversidge lectureship demand that the lecturer should " point out the directions in which further research work is desirable," I will try to indicate the lines on which chemical research on transmutation would seem at present to be most promising.

Let us first consider the *radiochemical methods.* I do not think that in the field of natural radioactivity many more radiochemical researches are necessary. There are no doubt still a few places in the disintegration series where the actual happenings are not well known, for instance, the beginning of the uranium and the actinium series, and it may further be that there are a few branch products and one or two—very feebly active—radioelements yet to be discovered; however, for chemists interested in radioactivity there are so many far more urgent problems that the elucidation of these minor points may well be postponed.

The really startling problems are those connected with the production of artificial radioelements. As new radioactive types of atoms can be created in almost every place of the periodic system, it needs a constant co-operation of chemists with physicists to identify the nature of these new atomic species. I have mentioned several cases where this collaboration has already resulted in the ascertainment of the equation of transmutation. But there are many processes where even now we are ignorant of the actual mechanism, and others which need further confirmation. Let me mention in this connexion only the very interesting discoveries of a radioactive isotope of helium, of a new radioactive series produced from thorium, and of elements with atomic numbers higher than that of uranium. The chemical nature of the radiohelium seems to be beyond doubt and only the atomic weight of this new helium isotope yet remains debatable, but the number and mode of production of four new radioelements from thorium, and of the five or so trans-uranium elements are still much in need of further radiochemical work. It may be emphasised that our conviction that elements with atomic numbers 93 to, probably, 97 have been formed is entirely based on radiochemical studies; simply because some of their analytical reactions are not to be found in the elements with atomic numbers up to 92 we are confident that the higher atomic numbers have been reached.

The reward for the by no means simple investigation on the trans-uranium elements will be not only the satisfaction of knowing the effect of neutron bombardment on the peculiarly unstable uranium nucleus but eventually knowledge of the chemical properties of elements so far not represented on our earth. Further, the more new radioactive isotopes of the ordinary elements are chemically identified, the richer becomes our store of " radioactive indicators " applicable to the solution of chemical and biological problems.

If we try to plan ahead what contribution purely *chemical methods* can make to questions of transmutation, we find that here the field of naturally occurring transmutations seems at least equally promising.

It is unlikely that amongst artificially produced elements the one example of a chemical detection mentioned above will remain unique. It might be useful to repeat some day the

same experiment with greater quantities of boron methoxide, thereby catching practically all the neutrons produced, and so obtaining a larger and better-defined amount of helium. Further, there will probably be no difficulty in proving by the same method the production of helium from lithium under neutron bombardment. Chemistry should be able to decide even questions inaccessible to physical methods; for instance, whether $^{8}_{4}Be$ is stable or disintegrates into two $^{4}_{2}He$ as soon as it is formed by the irradiation of $^{9}_{4}Be$ with γ-rays—a problem in the study of which we are engaged at present. But if we remember what has been said about the limits of practical detection of elements, we can at present hardly hope chemically to deal with other products of artificial transmutation besides the elements helium and neon. Of course, if we do not use neutron sources but collaborate with physical laboratories, the amount of artificially produced elements can be greatly increased; however, the bigger and more complicated the apparatus for producing the new elements, the harder it will be for the chemist to avoid contamination. If the product of disintegration should be an atomic species not represented in Nature, only then might its isolation be effected in spite of the difficulties of excluding impurities. If, for example, a helium isotope of atomic weight 3 or 5 could be artificially produced to an amount of 10^{-7} c.c. or so, it should be possible to separate it from all other gases besides the ordinary helium 4, and to detect its presence therein by the methods of interferometric spectroscopy; especially by using E. O. Lawrence's cyclotron—which produces a beam of accelerated particles outside the apparatus—should a sufficiently rigorous exclusion of ordinary helium be possible.

While, as we see, the application of chemical methods to artificial transmutations is not too easy, it seems quite likely that several modern microchemical methods are sensitive enough for use in the study of natural transmutations which constantly occur on our earth but so far have remained obscure. It has frequently been supposed that the property of spontaneous transmutation is not confined to the three radioactive series and the three isolated radioelements potassium, rubidium and samarium, but that other elements also may undergo a change, only too slowly to emit ionising rays. Here, of course, no radiophysical or radiochemical methods can be of any use; but a study of the quantities of elements associated in minerals can lead to the discovery of such hidden processes.

Let us imagine that the discovery of radioactivity had not taken place in 1896. It is well known that it was due not to any systematic development but to a piece of good luck. Because H. Poincaré had supposed that the origin of X-rays is connected with the fluorescent spot on the glass walls of the Roentgen tube, H. Becquerel investigated the effect of a fluorescent uranium salt on a photographic plate and discovered the invisible rays emitted from uranium. To-day we know that in the case of neither the X-rays nor the uranium rays has the fluorescence—which was the connecting link in the discovery—anything to do with the invisible rays; and it is, therefore, not without interest to speculate if, and when, radioactivity would have been discovered without this happy accident.

I think that only a few years later a systematic development of the chemical analysis of rocks would unavoidably have led to the discovery of transmutation processes going on in the earth's crust. As early as 1888 F. W. Hillebrand had described the surprising presence of an inert gas in certain minerals; it was supposed to be nitrogen, but after the discovery of argon (January, 1895) a re-examination of its nature seemed advisable. Simultaneously (April, 1895) this work was carried out in Ramsay's laboratory in London and in Cleve's laboratory in Upsala and the inert gas was identified as helium. A further study of the peculiar occurrence of a gas without chemical activity in certain minerals ought to have led in a perfectly logical way to the recognition that this inert gas could only have been formed after the solidification of the minerals; and the constant presence in these minerals of the heavy elements uranium or thorium or both would have suggested a genetic relation. (Hillebrand had already noticed the parallelism between gas- and uranium-content!) Probably even the dependence of the amount of helium on the age of the minerals would have been recognised after more extended researches, and by the next systematic step, namely, the laboratory study of the production of helium from uranium and thorium salts, even the order of the velocity of the helium formation from both these elements could have been discovered—without any knowledge of the rays emitted by radioactive substances!

I have sketched this imaginary line of development to make it clear that purely chemical researches may perhaps be able to detect transmutation processes which are actually going on without the emission of detectable rays. It seems very likely at present that one such process is already known in its outlines. In 1908 Lord Rayleigh discovered that the mineral beryl contains helium, although neither thorium nor uranium is present in sufficient quantity to account for it. Many rather far-fetched hypotheses have been formulated in explanation, for instance, the presence in beryl of channels in the crystal lattice, just large enough to permit the entrance of helium from the air, and the like. In 1926, after developing methods for the detection of very small quantities of helium, we tested another possibility, namely, the rayless formation of helium in beryllium salts, but by reason of difficulties of procedure our experiments were not conclusive. They have twice been started again, in Berlin and in Königsberg, but in both cases I had to leave the laboratory before a sufficient time for the accumulation of the helium had elapsed, and the delicate glass apparatus could not be transported. In 1933 a paper by Lord Rayleigh, attacking the problem in a more indirect way, made it very probable that the formation of helium in beryl must be due to some sort of atomic disintegration, as he proved that the younger minerals usually contain small, but the oldest formations relatively large, amounts of helium. While, however, the mean helium values of the beryls, grouped according to geological periods, show a decrease from Archæan to Tertiary, there is a very strong overlap, due perhaps to the fact that only a fraction of the helium has been retained in the minerals. In spite of the indirect evidence already available it is therefore by no means superfluous to examine directly the spontaneous production of helium from beryllium. About two years ago, with the help of Mr. J. W. J. Fay, I began these experiments for the fourth time, on a broader basis, and on this occasion I hope to reach definite results.

It might here be mentioned that a precision measurement of the development of helium from uranium and thorium salts is at present probably the best method of determining the disintegration constants of these long-living radioelements, which so far have been deduced from more indirect observations. Work on these lines is also in progress in my laboratory.

Not only beryllium but also potassium minerals frequently contain helium, but no uranium or thorium in sufficient quantity to account for its presence. Here O. Hahn has suggested that during the crystallisation of the mineral a fairly short-living helium-producing radioactive substance, radium *D*, was included, which has in the meantime decayed. This is one possible explanation of the presence of helium; but it is certainly desirable to confirm or exclude the alternative contingency of a helium-decay of potassium itself. Attempts in my laboratory in 1928 to discover a helium production in potassium salts were entirely negative and so already gave a maximum value of the velocity of such a hypothetic process; the amount of helium produced per year from 1 gram of potassium is less than 5×10^{-12} c.c. (uranium produces $1{\cdot}4 \times 10^{-8}$ c.c.).

There is also a special reason why it is desirable to have a complete knowledge of all transmutation processes going on in minerals by which helium might be produced. For geological age determinations the " helium method " is at present the most valuable of all. As this is an instance of a chemical study of transmutation processes useful also to other sciences, a reference to it is certainly not out of place in this lecture. Here is the principle: We know the velocity of disintegration of uranium and thorium, and also that the stable end products of both these radioelements are lead and helium; by measuring the quantities of uranium and thorium in a mineral, and of one of the end products, lead or helium, it is possible to determine the time which has elapsed since the mineral's solidification. As we now know how to determine very small quantities of helium, the " helium method " has the great advantage over the " lead method " of being applicable not only to radioactive minerals in the strict sense but to practically every rock of every geological period (which always contain traces of uranium and thorium). A former co-worker of mine, Dr. Urry, now at the Massachusetts Institute of Technology, has for years devoted his energy to geological age determinations by the helium method; and from the latest report of the Committee on the Measurement of Geological Time, edited by leading American geologists, chemists and physicists, it is obvious that Urry's work has been the most valuable contribution to geological time determination during the last year. The same

method applied to meteorites has already yielded results of interest to astronomers, and we may expect that in future many more workers will make use of it. Now it is obvious that a helium development from elements outside the uranium and thorium series would, as soon as established, necessitate special precautions and perhaps slight corrections. But at present there is no reason to doubt the reliability of the results obtained.

It would take too long to discuss here other cases where a careful chemical analysis of the elementary composition of minerals, or of the generation of new elements in salts, will be able to throw light on rayless transmutation processes continuing for geological periods. In many cases the analytical methods are not yet sufficiently developed and the limits of identification of the suspected elements remain behind the necessary sensitivity by several orders of magnitude. But it will certainly be worth while to pay attention to all cases where an especially careful micro-analysis might be able to discover processes of disintegration.

By all these researches we can hope to contribute in a small measure to the solution of a problem which has interested mankind for ages: the question of the evolution of our chemical elements. In the past century "evolution" was one of the leading ideas of the biological sciences, but few were inclined to apply this conception to inorganic matter. In earlier centuries no such dividing line was drawn, and to-day science has returned to a discussion of the genesis problem of the chemical elements. Even before the days of radioactivity the periodic system indicated some sort of relation between the elements, and many of you will remember the rather fanciful hypotheses which were suggested. In this country the best known is probably Crookes' idea of a building-up of all the elements from a very light primordial matter, "prothyl," by some sort of condensation process. However, the first experimental fact about the genesis of elements seemed flatly to contradict this, as the natural radioactivity revealed only disintegration, the breaking up of heavy elements into lighter ones. But since the discovery of the changes following atomic bombardment, especially since the production of artificial radioelements under the impact of neutrons, we know that all sorts of processes are actually occurring; the product of a transmutation may equally well be lighter or heavier than the original element (see Table I).

It seems certain that similar processes, of much greater intensity and variety, occur in stars. What we are accustomed to call "artificial radioactivity" is no more than a poor copy of some of Nature's performances, *e.g.*, in the interior of the sun, where under a pressure of a thousand million atmospheres and a temperature of about twenty million degrees the atoms of the elements are crushed. Under these extreme conditions the "law of conservation of the chemical elements" breaks down completely; all matter is changed into a sort of gas consisting of reactive nuclei and electrons. Out of the almost infinite variety of nuclei formed, only those can be found on our earth which, owing to their stability or long half-value period, have survived since the time when the earth separated from the sun; *i.e.*, the permanent atomic species and uranium, actino-uranium, thorium, potassium, rubidium and samarium. The others have decayed, and can only be "artificially" revived in our laboratories to their ephemeral life. There is, however, no intrinsic difference between them and the others, and it is even certain that occasionally in our cold earth transmutation processes occur outside the above-mentioned six radioelements and their families. For example, Dr. Hevesy has recently pointed out that the mineral gadolinite contains amongst other elements uranium, thorium, beryllium and gadolinium; as the mixture of uranium, thorium and beryllium must produce neutrons, and as the gadolinium nucleus is the strongest absorbent for slow neutrons we know, the heavier isotopes of gadolinium must have increased since the solidification of gadolinite, thereby slowly changing the combining weight of this rare earth. In other cases, as a consequence of neutron bombardment, new elementary species must be formed right in the minerals; also it is possible that the cosmic rays exercise some small influence on the stability of elements in our earth's crust.

So we see that even the old alchemistic idea of the growth of metals in mines is after all not so very far from the truth. Although it is not likely that these changes can at present be experimentally investigated, we may well hope that future refinements in the micro-analytical methods will open new possibilities for chemists to contribute to the study of transmutation.

The Principles of Distribution of Chemical Elements in Minerals and Rocks.

THE SEVENTH HUGO MÜLLER LECTURE, DELIVERED BEFORE THE CHEMICAL SOCIETY ON MARCH 17TH, 1937.

By PROF. DR. V. M. GOLDSCHMIDT.

WHEN, eight years ago, I had the honour of presenting a lecture ("The Distribution of the Chemical Elements," Friday Evening Lecture, March 15th, 1929) in this same room before an audience of the Royal Institution concerning geochemical research work at the University of Oslo, I explained some views on a problem, the study of which is interesting both for chemists and geologists, namely, the distribution of the chemical elements. I then gave some outlines of the problems involved, and also described examples of systematic relations.

Meanwhile, the general programme for geochemical research work indicated then has largely been followed; results have been obtained concerning the actual amount and distribution of nearly all the chemical elements, this having, in many cases, been rendered possible by new and improved methods of analysis. At the University of Göttingen, during the years 1929—1935, continuing and extending previous work at Oslo, I again had the privilege of co-operating with a number of young mineralogists, chemists, and physicists engaged in the problem of determining the composition of minerals and rocks, especially with regard to rare constituents.

For many years the methods of spectrographic analysis had been of great utility in ascertaining the presence of rare elements—I need only mention in this connection the important work in your country of Sir William Crookes, of W. N. Hartley, and H. Ramage. More recently, improved methods, in many cases combining chemical and optical work, have made it possible to collect numerous data with regard to the exact amounts of the constituents, through a large range of percentages.

During the first years of my research work, analysis by means of *X*-ray spectra, initiated by my friend Professor A. Hadding of Lund (Sweden), made possible several investigations upon rare constituents of minerals down to 0·1% or even to 0·01%; and during the Göttingen years, in co-operation with Dr. R. Mannkopff, assisted by a number of young research workers, methods of quantitative analysis by means of the arc spectrum were developed so as to be capable of determining 0·001% (or even less) of most elements. Apart from the publications of Dr. Mannkopff, I have to mention the work of my young friends Drs. Peters, Bauer, von Engelhardt, Hörmann, Noll, Minami, Strock, and Witte in developing and improving the new methods of analysis and co-operating in the collection of data. Of course, during our work the general advance in optical spectrographic methods, especially through the work of Professor Walther Gerlach in Munich, has been of much importance.

Our methods of analysis, either by physical means, such as optical and *X*-ray spectra, or by quantitative chemical work, have generally been directed to the development of those methods which permit the detection and determination of small amounts of various elements in rather small amounts of substance. We have purposely avoided those methods involving the working up of considerable amounts of substance, for the following reason: if we have to determine the distribution of substances between minerals of different kinds, particularly if very small percentages are involved, we have to take care that we really are studying the single pure mineral, and not a mixture containing contaminations from other minerals. This end is most readily attained if only small amounts of any mineral are needed for examination; as soon as we have to work up many grams or even kilograms, in most cases it becomes almost impossible to secure pure material for analysis.

Much has been said recently about the so-called "omnipresence" of all chemical elements, the supposed common level of the presence of a given element in any matter, especially in minerals. I feel sure that much, if not all, of this "omnipresence" of elements in crystallised minerals is due to their contamination by inclusions, surface adsorption, and other accidential impurities. In rocks, however, the omnipresence of elements has a reasonable meaning.

One great advantage of using only small amounts of substance for our investigation is

that one avoids the introduction of large amounts of laboratory reagents. The degree of impurity of even so-called fine chemicals is often astonishing, and in several cases we have found that in traditional methods of analytical determination of minor constituents a higher percentage of, for instance, barium has been contributed from the reagents than from the rock specimen.

Our methods of analysis have in many cases been founded on optical spectrography, based on the intensity of spectrum lines in the carbon arc, the Mannkopff–Peters effect of ionic concentration in the surface layer of the negative electrode being particularly used. Optical spectrographical methods also have been invaluable in the control of purity of reagents and efficiency of chemical separations.

Abundance of Elements.

		Earth's crust (g. per ton as unit).	Sun's atmosphere (0·1 mg. per sq. metre as unit).*			Earth's crust (g. per ton as unit).	Sun's atmosphere (0·1 mg. per sq. metre as unit).*
1	H	—	6,000,000	44	Ru	—	5
2	He	—	800,000	45	Rh	0·001 (G)	0·3
3	Li	65 (G)	0·6	46	Pd	0·01 (G)	1·2
4	Be	6 (G)	0·6	47	Ag	0·1 (G)	1
5	B	3 (G)	300 ?	48	Cd	0·5 (G)	15
6	C	—	300,000	49	In	0·1 (G)	0·1
7	N	—	500,000 ?	50	Sn	40 (G)	2
8	O	494,000	3,200,000	51	Sb	1 ?	1
9	F	270	—	52	Te	—	—
10	Ne	—	—	53	I	0·3 (L)	—
11	Na	28,300	400,000	54	X	—	—
12	Mg	21,000	1,500,000	55	Cs	7 (G)	—
13	Al	88,200	60,000	56	Ba	390 (G)	250
14	Si	276,000	600,000	57	La	19 (G)	8
15	P	786 (G)	—	58	Ce	44 (G)	40
16	S	500	—	59	Pr	5·6 (G)	1
17	Cl	480	—	60	Nd	24 (G)	15
18	Ar	—	—	61	—	—	—
19	K	25,900	250,000	62	Sm	6·5 (G)	5
20	Ca	36,300	200,000	63	Eu	1·0 (G)	4
21	Sc	5 † (G)	200	64	Gd	6·3 (G)	2
22	Ti	6,300	8,000	65	Tb	1·0 (G)	—
23	V	100	5,000	66	Dy	4·3 (G)	6
24	Cr	200	25,000	67	Ho	1·2 (G)	—
25	Mn	930	40,000	68	Er	2·4 (G)	0·2
26	Fe	51,000	1,000,000	69	Tu	0·3 (G)	—
27	Co	40 (G)	25,000	70	Yb	2·6 (G)	—
28	Ni	100 (G)	60,000	71	Cp ‡	0·7 (G)	—
29	Cu	100	6,000	72	Hf	3·2 (H)	0·4
30	Zn	40 (G)	5,000	73	Ta	—	—
31	Ga	15 (G)	6	74	W	69 (H)	0·3
32	Ge	7 (G)	80	75	Re	0·001 (N)	—
33	As	5	0·3	76	Os	—	—
34	Se	0·6 (G)	—	77	Ir	0·001 (G)	0·1 ?
35	Br	—	—	78	Pt	0·005 (G)	8
36	Kr	—	—	79	Au	0·005 (G)	—
37	Rb	310 (G)	4	80	Hg	0·5 (S)	—
38	Sr	420 (G)	150	81	Tl	0·3 (G)	5 ?
39	Y	31 (G)	30	82	Pb	16 (H)	3
40	Zr	190 (H)	30	83	Bi	0·2 (G)	—
41	Nb	15 (G)	1				
42	Mo	15 (H)	3	90	Th	11 (G)	—
43	Ma	—	—	92	U	4	—

G, data determined in the laboratories of the Mineralogical Institutes of Göttingen and Oslo; H, data determined by Prof. von Hevesy and co-workers; L, determination of iodine in rocks by G. Lunde; N, data of I. and W. Noddack; S, determination of mercury in rocks by Prof. A. Stock.

* Data due to H. N. Russell (*loc. cit.*). The data for H, He, and O are possibly somewhat too low. The elements P, S, Yb, and Cp have since been found in the sun's atmosphere.

† The data for scandium are under revision; our earlier estimate, 5 g., is possibly too low.

‡ Cp = Lu.

Much work had to be done in the development of methods, in the purification of electrodes, in finding standards of comparison, and, in many cases, in combining suitable methods of chemical concentration with a spectrographic examination of the concentrates.

The abundance of most elements in the surface matter of the earth is now known with some degree of accuracy. The preceding table demonstrates our present knowledge with regard to the rocks of the earth's surface as far as reliable data are available; these data are based partly upon the pioneer work of Clarke and Washington, and partly upon later investigations with regard to rare elements, many having been found at the Göttingen laboratory, others at Oslo, and others by von Hevesy and his co-workers or by I. and W. Noddack.

I have omitted data for hydrogen, carbon, nitrogen, and inert gases, as they are not significant for the analyses of the primary rocks, the hydrosphere and atmosphere being neglected.

A few years ago, the results of a chemical analysis of a composite sample of magmatic rocks were published by I. and W. Noddack (*Svensk Kem. Tids.*, 1934, **46**, **173**), and in many cases they agree with other determinations, but for certain elements (Y, Rh, Ir, Pt) their data appear to be decidedly too high, and for others (Co, Rb, Sr, Nb, Ag, Sn, I) they are lower than our data. The special assemblage of their composite sample of rocks may be the cause of some of the differences.

A most interesting basis for comparison between terrestrial and cosmic matter is given in Russell's data on the composition of the sun's atmosphere (*Astrophys. J.*, 1929, **70**, 11).

If we examine the results concerning the material in the surface rocks of the earth, we find that some elements are present in large percentages, such as silicon, aluminium, magnesium, and potassium; others are rather rare, *e.g.*, zirconium, scandium, beryllium, and rubidium; and some exceedingly rare, *e.g.*, platinum metals and gold, or selenium.

One of the most important problems in geochemistry is to find the true relative abundance of the chemical elements in the world as a whole, and from that point of view it is interesting to test whether the relative amounts of the elements in the earth's crust are truly representative of their primary proportions or whether these amounts have been modified by selective elimination of certain elements or groups of elements.

As I mentioned in my previous lecture (*loc. cit.*), some very suitable elements for a study of selective behaviour are those of the platinum and palladium families, or even the entire group of the precious metals. These metals are very rare in the earth's crust, and even 15 years ago, in a lecture at Leipzig, I had ventured the hypothesis that this rarity had been caused by a process of selective concentration into the interior of the earth, owing to the

Precious Metals in Meteoric Iron (Goldschmidt and Peters).

		G. per ton.							
Locality.	Structure.	Ru.	Rh.	Pd.	Ag.	Os.*	Ir.	Pt.	Au.
Coahuila, Mexico	Hexaedrite	10	5	10	5	?	10	10—100	5—1
São Julião de Moreira, Portugal	Octaedrite *cc*	10	10	10	5	5	1	10—100	10
Mount Joy, Pa., U.S.A.	,,	5—10	5	10	5	<5	1	10—100	5—10
Arispe, Mexico	,,	10	5	10	5	?	10	10—100	5—1
,, ,,	,,	10	5	10	1—5	5	10	10—100	5
Corrizatillo, Chile	,,	5	5	10	5—10	<5	5	10	5—10
Magura, Czechoslovakia	Octaedrite *c*	10	5	5—10	5	<5	5	10—100	5
Cañon Diablo, Ar., U.S.A.	,,	10	5	5—10	5	5	5	10—100	5
Rust Crust, Cañon Diablo	,,	10	5	5	1	5	5	10	5
Cranbourne, Victoria, Australia	,,	10	5	10	1	—	5	10	5
Rust, Cranbourne	,,	10	5	10	10	—	—	10	5
Savik, Cape York, Greenland	Octaedrite *m*	10	5	5	10	<5	10	10—100	5
Toluca, Mexico	,,	5	0·5	10	1	—	1	1	10
,, ,,	,,	10	5	10	1	—	1	10	10
Henbury, Central Australia	,,	10	5—10	10	5	5	10	10—100	5
N'Goureyma, Sudan	Octaedrite *b*	5	1—5	5	1	—	1	5—10	1
Morradal, Norway	Ataxite	5	5	10	5	—	1	10	5
,, ,,	,,	5	5	10	1—5	<5	1	10—100	5—10
Capland	,,	10	5—10	10	5—10	5	10—100	100—10	1
Rust Crust, Hoba, S.W. Africa	,,	10	5—10	10	1	<5	10	100—10	0·5
,, ,, ,, ,,	,,	10	5—10	10	1	5	10	100—10	0·5
Medwedewa, Krasnojarsk, Siberia	Iron from pallasite	5	5	10	5—1	—	—	5	5
,, ,,	,, ,,	5	1—5	10	1—5	<5	1	5	5
Brenham, Kansas, U.S.A.	,, ,,	5—10	5	10	1	<5	5—1	10—100	10—5
Estherville, Iowa, U.S.A.	Iron from siderolite	10	5	10	1	<5	1	*10*	1—5
Knyahinya, Czechoslovakia	Iron from chondrite	10	5	10	5	<5	·5	10—100	10
Holbrook, Arizona, U.S.A.	,, ,,	10	10	10—100	1	<5	5	100—10	10

* The data for osmium are minimum amounts, as part of the metal is lost as volatile OsO_4.

large partition ratios of these metals between silicate slags and iron alloys, and I recommended a systematic search for the platinum metals in meteoric irons. Eight years ago I was able to give many new examples to demonstrate the abundance of platinum metals in meteoric iron, and to-day our question can be answered in much greater detail by a number of analyses of meteoric irons for platinum metals; these were made partly in the Göttingen laboratory, and partly by I. and W. Noddack in Berlin. The table on p. 657 gives the data from Göttingen.

The following table averages the data from Göttingen and from Berlin.

Meteoric Iron (Average).

Precious metals, g. per ton.

	G. and P.	I. and W. Noddack.				G. and P.	I. and W. Noddack.		
	1932.[1]	1930.[2]	1931.[3]	1934.[4]		1932.[1]	1930.[2]	1931.[3]	1934.
Ru	10	23·9	20·30	12—13	Os	>3	8·8	25·30	9
Rh	5	5·0	4	4—5	Ir	5	2·3	5	3·6
Pd	10	19	15—20	10—11	Pt	20	17·7	10—22	23
Ag	5	3·2	6—8	3—4	Au	5	1·4	0—1	2—3

[1] Goldschmidt and Peters, *Nachr. Ges. Wiss. Göttingen, Math.-phys. Kl.*, 1932, 377.
[2] *Naturwiss.*, 1930, **18**, 757.
[3] *Z. physikal. Chem.*, 1931, *A*, **154**, 207; *ibid.*, Bodenstein-Festband, 1931, 890.
[4] *Svensk Kem. Tids.*, 1934, **46**, 173.

From the tables, we see that concordant data exist with regard to the amounts of platinum metals in meteorites, and that these are in full agreement with prediction. A very interesting result of investigations during recent years is our discovery that gold also is concentrated in meteoric iron in very considerable amounts. If the nucleus of the earth is as rich in gold as the average meteoric iron, about 5 g. per ton, then the interior contains enough gold to make a coating of the metal 1 m. thick over the entire surface of our globe.

Still another element which has hitherto been considered as very rare has been found by us in large amounts in meteoric iron: that is germanium. We have found this in small amounts (a few g. per ton) in all terrestrial and meteoric silicate rocks,* but most of the germanium in the world has been concentrated in certain metallic alloys, such as meteoric iron. The following table affords a comparison between the concentrations (in g. per ton) in the earth's crust and in meteoric iron.

	Earth's crust.	Meteoric iron.	Factor.		Earth's crust.	Meteoric iron.	Factor.
Pt	0·005	20	4000	Au	0·005	5	1000
Ir	0·001	5	5000	Ni	100	80,000	800
Rh	0·001	5	5000	Ge	7	500	70
Pd	0·01	10	1000	Ag	0·1	5	50

Now, we can further test our hypothesis concerning the distribution of precious metals and of germanium by means of experiments which Nature itself has performed. If our silicate rocks have been deprived of precious metals and of germanium by some process of equilibrium of partition between silicate slag and iron alloy, then we could reproduce practically the same equilibrium by bringing a large amount of fused silicate rock into contact with a very small amount of metallic iron, and we should expect concentration of the same rare elements in the iron as have been concentrated in iron meteorites. Such experiments which establish the equilibria of partition between large amounts of fused silicate and small amounts of iron have been made by Nature in the cases of the iron lumps in the basalt of Ovifak, on the island of Disco, near Greenland, and of the iron-nickel alloy josephinite in olivine rock from Oregon, U.S.A. The following data demonstrate that precious metals and germanium have been concentrated effectively in the Ovifak iron, and our investigation of precious metals in josephinite revealed about 5 g. of platinum, 10 g. of palladium, and 1 g. of gold per ton, besides much silver.

* Important observations on the occurrence of germanium in certain silicates have been made also by J. Papish.

Iron from Basalt, Ovifak, Disco, Greenland (g. per ton).

Pt.	Pd.	Rh.	Ru.	Au.	Ag.	Ge.
5	1	0·5	0·5	5—1	5—10	1000

We may take these data as a confirmation of our hypothesis that equilibria of partition between metallic or semi-metallic phases and silicate phases have been responsible for a more or less effective elimination of certain elements from the material of the earth's crust. We may summarise our knowledge concerning these equilibria in the following table, where the first three columns refer to the equilibria of partition between liquid iron, liquid sulphides, and fused silicates.

Iron, siderophile.	Sulphide, chalcophile.	Silicate, lithophile.	Gases, atmophile.	Organisms, biophile.
Fe, Ni, Co	((O)), S, Se, Te	O, (S), (P), (H)	H, N, C, (O)	C, H, O, N, P
P, (As), C	Fe, Cr, (Ni), (Co)	Si, Ti, Zr, Hf, Th	Cl, Br, I	S, Cl, I (B)
Ru, Rh, Pd	Cu, Zn, Cd, Pb	(Sn)		(Ca, Mg, K, Na)
Os, Ir, Pt, Au *	Sn, Ge, Mo	F, Cl, Br, I	He, Ne, Ar	(V, Mn, Fe, Cu)
Ge,* Sn *	As, Sb, Bi	B, Al, (Ga), Sc, Y	Kr, X	
Mo, (W)	Ag, (Au), Hg	La, Ce, Pr, Nd, Sm		
(Nb), Ta	Pd, Ru, (Pt)	Eu, Gd, Tb, Dy		
(Se), (Te)	Ga, In, Tl	Ho, Er, Tu, Yb, Cp		
	(Cr)	Li, Na, K, Rb, Cs		
		Be, Mg, Ca, Sr, Ba		
		(Fe), V, Cr, Mn		
		((Ni)), ((Co)), Nb, Ta		
		W, U, ((C))		

* That germanium, tin, and gold are distinctly siderophile elements has recently been proved by independent studies on meteorites and on metallurgical products.

The principle of partition of elements between a metallic liquid, rich in free electrons, a sulphidic liquid of a semi-metallic nature, and an ionic liquid affords a classification in three groups of elements, with regard to their geochemical affinities, these three groups being accompanied by a fourth, including the elements which are accumulated in gas phases, either as free volatile elements or as gaseous compounds. A fifth group contains those elements which are concentrated by living organisms in later stages of terrestrial evolution.

The partition of elements according to the first four groups of geochemical affinity is closely related to the structure of the electron shells of the atoms. Ions of the rare-gas type, *e.g.*, those of sodium, calcium, and aluminium, enter preferentially into the ionic phases of the silicate shell; the metallic elements of the transition groups, such as nickel, palladium, and platinum, enter preferentially into the iron alloys; and elements of the 18-electron shells, such as copper, lead, etc., into sulphide melts, if the potential of reduction is not high enough to permit formation of their iron alloys. A corresponding classification of all elements in two groups, metallogenetic and petrogenetic, was proposed by Washington in 1920.

The classification into the groups of different geochemical affinity, a division connected with potentials of ionisation and with the type of ionic structure, is not exclusively restricted to the time of the formation of the principal shells of the earth, but may take place at any time when an element has to be distributed between ionic, metallic, and semi-metallic phases. Therefore, we find iron, nickel, and gold in native platinum, and nickel, copper, and platinum metals in iron monosulphide ores, and I think that even the concentration of gold in pyrites and in arsenopyrites may be an analogous process of concentration of siderophile precious metals in semi-metallic phases. In this connection, it may be interesting to note that gold and even platinum metals have been concentrated in hydrothermal nickel arsenide minerals, as might have been expected.

Of course, the quotients of distribution into the primary geochemical affinity groups are dependent on the temperature; also, the degree of reduction of the system is often of importance. For instance, chromium is a strongly lithophile element under ordinary terrestrial conditions. If, however, oxygen is deficient, as in iron meteorites, chromium is decidedly chalcophile, entering almost exclusively into the sulpho-spinel daubréelite, $FeCr_2S_4$.

Our first principle of geochemical distribution, the principle of the four primary geochemical affinity groups, accounts for the scarcity of certain elements in the earth's crust, and its validity has been verified by us and others by means of analyses of the different phases of meteorites.

In comparing the composition of meteorites with that of the earth's crust, we have to distinguish between three different assemblages of elements in the meteorites; as pointed out in my 1929 lecture, these are the silicates of the stony meteorites, the iron–nickel alloy of the iron meteorites and of the stony meteorites, and the sulphide phase (troilite) of both. Our knowledge of the relative abundance of elements in meteorites is due mainly to the early compilations of Farrington and of Merrill, and to numerous determinations of rarer elements in the Göttingen laboratory and by I. and W. Noddack, von Hevesy, Paneth, and others.

An important verification of our geochemical classification has been obtained by the study of certain metallurgical products from the copper industry of the Mansfeld district in Germany; Cissarz and Moritz have studied the sulphide phase, the pig iron and the silicate slags from Mansfeld, and have found a distribution of elements representative of the partition into the corresponding geochemical groups. It may be noted that the elements gold, tin, and germanium, once considered by me to be dominantly chalcophile, have been found to be siderophile with regard both to behaviour in industrial separation and to separations in meteoric matter.

We understand clearly why the typical siderophile and chalcophile elements are only sparsely represented in the silicate crust of the earth, and how they are distributed between minerals of different bond type, and our knowledge has advanced so far as to permit a successful prediction of hitherto unknown modes of occurrence. The processes of mineral formation and of the partition of elements between different minerals are, however, not limited to the separation of metallic, semi-metallic, and ionic substances, for a number of other mineral-forming and differentiating processes have been, and still are, operating.

The processes mentioned above have not been directly connected with or restricted to the crystalline state of matter. The partition into chalcophile and lithophile elements takes place between amorphous, liquid phases, as well as in interactions in which crystalline substances are involved. We shall now, however, study some processes which are directly related to properties of crystalline matter, *i.e.*, the processes of formation of crystallised minerals from liquid or gaseous systems.

The formation of crystalline minerals involves the building up of space lattices of atoms or ions, in a regular arrangement, depending upon the size, or we may say the radii, of the individual atoms or ions. Into such a lattice only those particles can enter which are of a size appropriate to the lattice spacings. Therefore the crystals act as a kind of sorting or sieving mechanism, allowing certain particles to enter, and excluding others of unsuitable size.

Any process which involves the formation of crystalline minerals, whether from molten magmas, from aqueous solutions, or from gases, involves a sorting of elements according to the radii of their atoms or ions, and one of the most important principles for the distribution of the elements, therefore, is the grading according to size, especially as compared with the lattice spacings or interatomic distances of rock-forming minerals of the most ordinary elements.

The following table gives a list of elements, or rather of their ions, arranged according to their radii. It is noteworthy that the importance of these dimensions for the connection between chemical composition and crystal structure emerged primarily from our geochemical work on the distribution of particles between crystalline minerals.

Radius, A.	Ions.	
0·1—0·3	B^{3+}, C^{4+}, N^{5+}, S^{6+}	
0·3—0·5	Be^{2+}, Si^{4+}, Ge^{4+}, P^{5+}, V^{5+}, Mo^{6+}, W^{6+}	
0·5—0·7	Al^{3+}, Ga^{3+}, Fe^{3+}, Cr^{3+}, V^{3+}, Ti^{4+}, Nb^{5+}, Ta^{5+}	
0·7—0·9	Li^{1+}, Mg^{2+}, Ni^{2+}, Co^{2+}, Fe^{2+}, Zn^{2+}, Sc^{3+}, In^{3+}, Zr^{4+}, Hf^{4+}, Sn^{4+}	} Mn^{2+}
0·9—1·1	Na^{1+}, Ca^{2+}, Cd^{2+}, Y^{3+}, Gd^{3+}—Cp^{3+}, Ce^{4+}, Th^{4+}, U^{4+}	}
1·1—1·4	K^{1+}, Sr^{2+}, La^{3+}—Eu^{3+}	
1·4—1·7	Rb^{1+}, Tl^{1+}, Cs^{1+}, Ba^{2+}, Ra^{2+}	

In the group of the lanthanides I have drawn the subdivision between Eu (radius 1·13) and Gd (radius 1·11) instead of between Gd and Tb, in order to follow the traditional division between cerium and yttrium earths.

Given a table of radii of ions, we can as a rule predict into which minerals any given element is entering; for instance, we may predict a connection between magnesium and a number of other elements:

Mg^{2+} 0·78, Li^{1+} 0·78, Ni^{2+} 0·78, Fe^{2+} 0·83, Co^{2+} 0·83, Sc^{3+} 0·83

Now the question arises as to the order of preference in which the different ions, being of suitable size, will enter into a crystal lattice: not all guests are equally welcome in a lattice, and the crystal in many cases makes a choice between them. Let us first consider the simplest case. In the pair magnesium–nickel the radii are alike, and also the charges of the ions, both metals being bivalent, and therefore the nickel ions pass into the crystals of magnesium silicate with about the same probability as the magnesium ions; consequently, the amount of nickel in a number of magmatic minerals is roughly proportional to that of magnesium.

If radii, charges, and the ionic type of two elements are exactly alike or very similar, then no separation takes place at all; I may refer to the pair zirconium–hafnium, known through the work of von Hevesy and Coster, or to the pair yttrium–holmium, which is never separated in Nature. The rare elements hafnium and holmium are hidden away by "camouflage" in minerals of more common elements (zirconium and yttrium).

If there is some small difference of ionic radius, the bond is weakened for the larger ion; therefore the melting point of iron olivine is lower than that of magnesium olivine, and the larger ion is concentrated in the mother-liquor as compared with the smaller ion according to the fusion diagram found by Bowen and Schairer. The following data illustrate the difference of melting points:

Mineral	Formula.	M. p.	Mineral.	Formula.	M. p.
Forsterite	Mg_2SiO_4	1910°	Fayalite	Fe_2SiO_4	1205°

Even small differences in radii may thus make possible an enrichment of the larger component of such a pair in late crystallates and in mother-liquors, as, for instance, in the pair aluminium–gallium, the radii of the tervalent ions being 0·57 A. (Al) and 0·62 A. (Ga).

	Ga_2O_3, %.	Al_2O_3, %.	Ga : Al (atoms).
Bytownite, Sogndal, Norway	0·0005	32	1 : 120,000
Nephelite, Langesund, Norway	0·01	32	1 : 6,000
Diasporite, Langesund, Norway	0·2	80	1 : 800
Opalised wood, Yellowstone Park, U.S.A.	0·1	0·7	1 : 13

Another example is furnished by certain univalent followers of potassium in *late* crystals of potassium minerals; for instance, in the potash felspars of pegmatites we find considerable amounts of rubidium, cæsium, and thallium, according to the relation of the radii of the univalent ions: K 1·33 A., Rb 1·49 A., Tl 1·49 A., Cs 1·65 A.

Now a crystal may extend its hospitality even to ions having a fitting radius but a different charge (of the same sign); for instance, magnesium minerals may take up scandium or lithium. In what sequence do such ions of different charge enter a crystal structure? We have found that this order depends upon the magnitude of the electrostatic charge of the ion, as long as simple atomic ions are concerned. The ion which has a larger charge has the preference over other ions of the same size but of lower charge For instance, the atoms of scandium enter into early crystallisations of magnesium minerals, especially into the pyroxenes of gabbros and basalts.

A very well-known analogous example is offered by the groups of soda–lime felspars, the plagioclases, the bivalent ions preferentially entering the crystal, and giving rise to the well-known crystallisation diagram of the lime–soda felspars as found by Bowen:

Mineral.	Formula.	M. p.
Anorthite	$Ca^{2+}(Al_2Si_2O_8)^{2+}$	1550°
Albite	$Na^{1+}(AlSi_3O_8)^{1+}$	1090

Therefore calcium is concentrated in early fractions of plagioclase crystals, sodium in late fractions.

In the same manner strontium and barium enter early crystals of potash felspars, as found by Noll and von Engelhardt at Göttingen. We have given the phenomenon the name of "capturing" ("Abfangen") of highly charged ions.

Correspondingly, ions of fitting radius, but having a *lower* charge are only reluctantly admitted into the same crystals, owing to correspondingly weakened electrostatic bonds. Therefore lithium is concentrated not in the first but in the *last* crystallates of magnesium minerals, as shown by the very accurate studies of Strock at Göttingen.

Quotient (by weight), $\frac{Li_2O}{MgO} \times 10{,}000$, *according to Strock.*

Early:	Peridotite	0·12	Early:	Basalt	3·3
	Pyroxenite	0·17		Porphyrite and andesite	16
	Gabbro	3·3			
	Diorite	10			
Late:	Syenite	20	Late:	Trachyte	150
	Nephelite syenite	70		Phonolite	140
	Granite	600		Liparite and obsidianite	200

Generally, in the series of magmatic rocks and minerals, these rules enable us to discriminate between elements of early and those of late introduction into the crystals of common rock-forming minerals. In the following table, the examples are taken mostly from investigations in collaboration with Dr. Bauer, Dr. Hörmann, and Dr. Witte; the barium data are due to Dr. von Engelhardt.

	Early.				Late.			
Rock.	Cr_2O_3, %.	NiO, %.	CoO, %.	MgO, %.	BaO, %.	Nb_2O_5, %.	La_2O_3, %.	K_2O, %.
Peridotite (dunite)	0·50	0·40	0·03	40	0·0003	—	—	0·1
Gabbro	0·05	0·02	0·01	8	0·007	0·001	0·001	1
Diorite	0·01	0·005	0·004	3	0·03	0·003	0·003	2
Granite	0·0003	0·0003	0·001	1	0·05	0·005	0·005	4
Nephelite syenite	0·0001	0·0003	0·001	1	0·06	0·02	0·05	6

If, now, we compare the chemical composition of the earth's crust and of silicate meteorites, we find the well-known differences clearly explained as a consequence of selective enrichment of late crystallates in the uppermost crust of the earth:

Grams per ton.

	Silicate meteorites.	Earth's crust.	Factor.	
Cr	3,200	200	0·06	Early crystallisation.
Mg	137,000	21,000	0·15	
Zr	80	190	2·3	Late crystallisation.
Na	3,700	21,400	2·5	
Li	5	65	13	
K	1,700	25,900	15	
Sr	20	420	21	
Ba	5	390	78	

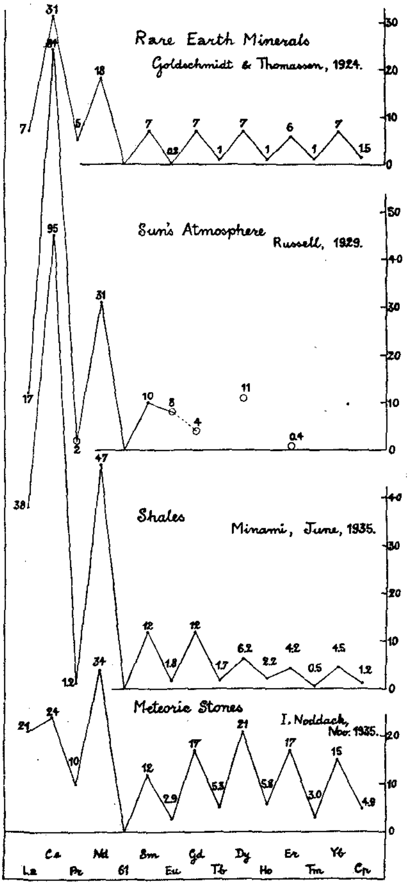
The enrichment of late crystallates in the uppermost crust of the earth is effected by the relatively low specific gravity of granite magmas, nephelite syenite magmas, and aqueous residual solutions, which all tend to migrate towards the surface of our planet.

In order to ascertain the original proportions between elements, we have to search for "coherent groups" of elements, *i.e.*, elements which, owing to their similarity in radius and in valency, enter into the same minerals at about the same stage of fractional crystallisation. Zirconium and hafnium are one such coherent pair. A large rather coherent group is furnished by the rare-earth elements, comprising the lanthanide family (elements of atomic number from 57 to 71) and yttrium.

The data in Fig. 1 embody determinations of the proportions of these elements, as

found in rare-earth minerals by me and Thomassen (*Vid. Selsk. Skr., Math. Naturv. Kl.*, 1924, No. 5), in the sun's atmosphere (still somewhat incomplete data) by Russell (*loc. cit.*),

FIG. 1.



in average samples of sedimentary rocks (shales) by my co-worker Minami, (*Nachr. Ges. Wiss. Göttingen, Math. Phys. Kl.*, 1935, 1, 155), and somewhat later in stone meteorites by

I. Noddack (*Z. anorg. Chem.*, 1935, **225**, 337): the coherency of the group is distinctly visible. All data are referred to 100 atoms of yttrium as the unit.*

Some differences are of interest. The relatively small amount of cerium, as compared with the tervalent rare-earth elements, given by I. Noddack for the meteorites may be caused, I think, by a partial loss of that element, probably in the separation of thorium, due to the hydrolytic precipitation of ceric hydroxide.

More interesting are the differences concerning the element europium. In rare-earth minerals this metal is usually present only in very minor amounts, even in comparison with other elements of odd atomic number. However, in the assemblage of rare-earth elements, which is found in sedimentary rocks and represents an integration or re-assembling of all the rare-earth atoms of primary minerals and rocks, europium is found in similar amounts to, for instance, terbium. Also, in the solar atmosphere as well as in many stellar atmospheres, europium is found in amounts not less than those of other odd rare-earth elements.

Unpublished investigations by me and Dr. Bauer at Göttingen have revealed terrestrial assemblages rich in europium, for instance in certain pyromorphites, many titanites, potash felspars, and some strontianites. Many years ago I predicted close isomorphism between bivalent europium and strontium, a prediction which has been verified by the Noddack's experimental work on the isolation of europium by means of mixed crystals of the sulphates at the Freiburg laboratory.

As a summary of all investigations on crystallised minerals of magmatic origin, we may state that the radii and valency properties of the atoms and ions regulate the distribution of elements in the primary magmatic rocks and in the minerals of those rocks. Also, these principles have made possible the prediction of unknown facts, and the systematic investigation of the composition of magmatic minerals and rocks with regard to minor constituents has greatly augmented our knowledge of geochemistry. I may mention the important comprehensive investigations made by Russian geochemists, especially A. E. Fersman.

As a third, *most important field of research, the geochemistry of sedimentary rocks* has been studied in more detail during the last eight years. The importance of this field of geochemistry may be judged by the fact that a very great percentage of ores and other useful minerals and rocks is associated with sediments. According to available statistical data, about 85—90% of the annual yield of mineral products comes from sedimentary mineral and ore deposits, and this fact emphasises the great practical importance of the geochemistry of sediments.†

The processes of weathering, transportation, and redeposition of matter at the surface of the earth's crust involve a great number of chemical reactions concerning all chemical elements. The importance of the geochemistry of sediments has long been recognised by Russian scientists, particularly Vernadsky.

For the processes in igneous rocks and their derivatives we have learnt to consider the effects of atomic and ionic properties, *e.g.*, ionic size and charge, as most important factors in the distribution of the elements. In the processes of sediment-making also, ionic size and charge are of the utmost importance, especially in a certain mutual relation, *viz.*, the ionic potential, given by the quotient between ionic charge, Z, and ionic radius, r. The importance of this function in physical chemistry has been demonstrated by Cartledge (*J. Amer. Chem. Soc.*, 1928, **50**, 2855).

Besides the ionic potential and the deformability of ions, their polarisability is of importance as a controlling factor in certain phenomena of ionic adsorption, as demonstrated by Noll.

We give a table and a graph (Fig. 2) illustrating the ionic potential.

The ionic potential is important not only for the distribution of chemical elements during the formation of sedimentary rocks, but also for other mineral-forming processes,

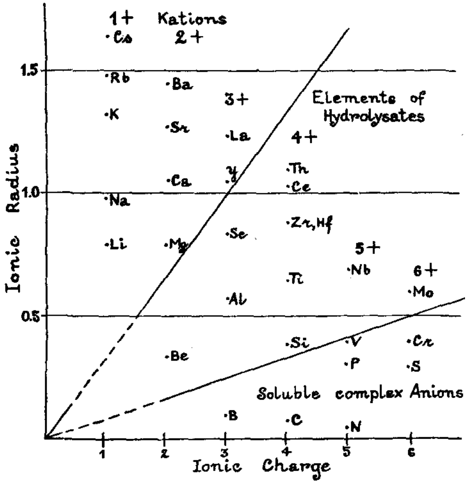
* Quite recently, data on the amounts of rare-earth elements in iron ores from Sweden have been published by Landergren (*Jernk. Annaler*, 1936, 711), which afford another welcome confirmation of the "geochemical coherency" of the rare-earth elements.

† For a number of ores the importance of sedimentary deposits has recently been pointed out by Brinkmann.

Ionic potential, Z/r.

Cs^{1+} 0·61	Rb^{1+} 0·67	K^{1+} 0·71	Na^{1+} 1·0	Li^{1+} 1·3	Ba^{2+} 1·4	Sr^{2+} 1·6	Ca^{2+} 1·9	La^{3+} 2·5	Mg^{2+} 2·6
Sm^{3+} 2·7	Y^{3+} 2·8	Cp^{3+} 3·0	Sc^{3+} 3·6	Th^{4+} 3·7	Ce^{4+} 3·9	Zr^{4+} 4·6	Al^{3+} 5·3	Be^{2+} 5·9	
Ti^{4+} 6·3	Nb^{5+} 7·3	Mo^{6+} 9·7	Si^{4+} 10	B^{3+} 15	P^{5+} 15	S^{6+} 20	C^{4+} 27	N^{5+} 45	

FIG. 2.



especially those connected with aqueous solutions. The same principle also regulates the base exchange of zeolite minerals: natural zeolite crystals collect ions the potential of which does not exceed 2·0.

The potential is very important also for the chemical behaviour of elements: I may mention the similarity of the hydrated ions of tervalent scandium and quadrivalent thorium, of bivalent beryllium and tervalent aluminium.

Substances with low ionic potential, such as sodium, calcium, and magnesium, remain in true ionic solution in the process of weathering and transportation; those with intermediate ionic potential are precipitated by hydrolysis, their ions being associated with hydroxyl radicals from aqueous solutions; and substances with still higher ionic potential form anions containing oxygen and usually again soluble to give true ionic solution. The field of elements is therefore divided into three parts with respect to ionic potential.

We can illustrate sediment-forming processes by the following classification of their products, showing the analogy between these processes and a chemical analysis.

Succession of sediments.

	Examples.
1. Residua	Quartz, zircon.
2. Hydrolysates	Bauxite, clays.
3. Oxydates	Limonite, psilomelane.
4. Carbonates	Calcite, dolomite.
5. Evaporates	Chlorides, sulphates, borates.

First of all, insoluble substances remain as residua, mostly as granular material which form sands, grits, etc. Next, the fine mud of hydrolysates settles down; it contains hydroxy-silicates or hydroxides of aluminium, finely divided micas and chlorites, and finely divided silica, forming clays, bauxites, shales, etc. Another stage consists in the precipitation of hydroxides of ferric iron and of tervalent and quadrivalent manganese; such precipitation has to be preceded by a process of oxidation, mostly in shallow surface waters, whereby the ferrous and manganous ions are converted into the higher state of valency, which has a much higher ionic potential, and this in turn causes precipitation. In a great many cases, such as in ordinary mudstones, the hydrolysates and oxydates are associated in the same sediment.

Our studies in Göttingen had as one principal aim to account for a quantitative balance of substances through the process of sedimentation. Following an early attempt by Joly (*Sci. Trans. Roy. Dublin Soc.*, 1899, **7**, 23), one can calculate the amount of matter in the sedimentary cycle by means of the sodium content of the ocean; calculation based upon our new material furnishes and uses the following data. For each kg. of sea water about 600 g. of primary rocks have passed through the cycle of weathering, disintegration, and sedimentation.

Amounts (kg.) of Rocks of Sedimentary Cycle and of Surface Waters per cm.² of the Surface of the Earth.

Shales and sandstones	155	Sea water	268·5
Limestone	10·2	Fresh water	0·1
Dolomite	4·4	Continental ice	4·5
Total	169·6	Water vapour	0·003

For a number of elements, *e.g.*, carbon and oxygen, we have attempted quantitative balances to account for the amounts involved and recovered. Here I shall only point out one single aspect of the balances, *viz.*, the amounts of several elements which have entered into and remained in solution in sea water.

Balance of Various Univalent, Bivalent, Tervalent, and Quadrivalent Metals in Sea Water, per Kg. of Sea Water.

	Supplied.	Present.	Percentage.		Supplied.	Present.	Percentage.
Na	16·8 g.	10·7 g.	66	Al	52·6 g.	0·6 mg.	0·0012
K	15·0 g.	0·37 g.	2·5	Sc	3 mg.	0·04 γ	0·0013
Li	39 mg.	0·11 mg.	0·2	Y	19 mg.	0·3 γ	0·0016
Rb	200 mg.	0·2 mg.	0·1	La	11 mg.	0·3 γ	0·003
Cs	6 mg.	0·002 mg.	0·03	Si	160 g.	1 mg.	0·0006
Mg	12·6 g.	1·3 g.	10	Ce	26 mg.	0·4 γ	0·002
Sr	250 mg.	10 mg.	4				
Ca	21·6 g.	0·42 g.	2				
Ba	23·4 mg.	0·05 mg.	0·02				

We shall first discuss elements of low ionic potential, beginning with the alkaline metals. We see that sodium alone remains to any great extent in the sea; potassium remains only in some few units %, owing to the very strong adsorption of its ions on the finely divided hydrolysate sediments. Still more effectively the *rare* alkaline ions are being eliminated from the sea water; also direct experiments have shown that rubidium and cæsium are adsorbed to a higher degree than potassium.

The same sort of balance for the bivalent alkaline-earth elements demonstrates that the amounts left in sea water are conspicuously less than the relative amounts of the alkaline metals. It is interesting that strontium remains in sea water to about double the extent of calcium.

A comparison of tervalent elements * with regard to marine concentration reveals that the rare-earth metals are somewhat favoured as compared with aluminium, probably owing to their smaller ionic potential. The presence of rare-earth metals in sea water is,

* This is based on some still unpublished investigations from the Göttingen laboratory concerning rare-earth elements.

of course, interesting in connection with the findings of Sir William Crookes concerning the presence of minute amounts of, *e.g.*, yttrium and samarium in the lime carbonate of marine organisms. In Göttingen, we have been able to prove the presence of all rare-earth metals in, for instance, the lime carbonate of corals or very pure chalk from Southern Sweden. In this connection I may mention that the calcites of mineral veins, too, always contain determinable amounts of rare-earth metals.

A study of some quadrivalent elements in sea water similarly indicates a preference for those elements having small ionic potentials. However, the ionic potential of these elements is generally so high that it causes almost quantitative precipitation with the hydrolysate sediments. For the same reason we find a number of rare quadrivalent elements concentrated in the hydrolysate sediments. For instance, besides beryllium and gallium, which follow aluminium, the elements titanium, zirconium, tin, and quinquevalent niobium are found to be concentrated in bauxite, together with aluminium hydroxide, and the factor of concentration is about the same as for that of alumina, being as a rule about 4—5-fold as compared with their mother rock.* In some cases vanadium also is somewhat concentrated in the bauxites. The tervalent elements with somewhat lower ionic potential, such as the lanthanides, yttrium, and even scandium, are as a rule not concentrated in typical bauxites, because their lower ionic potential permits their removal in aqueous solutions.

Balance of Various Elements forming Anions in Sea Water, per Kg. of Sea Water.

	Supplied.	Present.	Percentage.		Supplied.	Present.	Percentage.
B	2·4 mg.	6 mg.	260	I	0·18 mg.	0·05 mg.	28
Cl	0·29 g.	19·3 g.	670	F	150 mg.	1 mg.	0·7
S	0·3 g.	0·88 g.	290	P	470 mg.	0·06 mg.	0·013

A study of the balance of the common anions in sea water, such as chloride, iodide, sulphate, and borate, reveals the very interesting fact that certain of these elements are found in sea water in such large amounts that a derivation from the primary rocks through weathering processes seems impossible. We are led to believe that chlorine, boron, and probably sulphur have been primary constituents of oceanic waters, for the amounts derived from primary rocks are smaller than the amounts present in the sea water of to-day, and the percentages of boron and sulphur in fossil sediments are so large that the proportion of these elements in the ocean was probably still higher in earlier geological periods than now. However, we have to consider the possibility of large supplies of chlorine, sulphur, and boron from volcanic gases and volcanic springs.

Balance of Various Heavy Metals and Metalloids in Sea Water, per Kg. of Sea Water.

	Supplied.	Present.	Percentage.		Supplied.	Present.	Percentage.
V	60 mg.	0·3 γ	0·0006	Hg *	0·3 mg.	0·03 γ	0·01
Mn	0·56 g.	4 γ	0·0007	Pb	10 mg.	?	?
Fe	31 g.	60 γ	0·0002	Cu	60 mg.	10 γ	0·017
Ni	60 mg.	0·07 γ	0·0001	Se	0·4 mg.†	4 γ	1
Mo	9 mg.	0·7 γ	0·008	As	3 mg.	20 γ	0·7
Zn	24 mg.	7 γ	0·03				

* Data by Stock and Cucuel (*Naturwiss.*, 1934, **22**, 391).

† From the selenium percentages in sedimentary rocks; the values from igneous rocks might probably be somewhat lower.

Important results are being obtained concerning the percentage of certain poisonous metals and metalloids in sea water. We find that the amounts which potentially have been supplied from the primary rocks to sea water during geological times are so considerable that a serious poisoning of the ocean would have been caused if some phenomena of elimination of poisonous substances had not been in action; this applies, for instance, to copper, lead, arsenic, selenium, and mercury.

We find that a number of poisonous elements, among them selenium, arsenic, lead,

* I may mention that the alkali aluminate solutions of the Baeyer process for making alumina are a potential source for very large quantities of gallium.

antimony, and bismuth, have been removed from aqueous solution by means of a process also known in practical medicine, that is, adsorption on freshly precipitated hydroxides of iron. We find considerable concentrations of selenium, arsenic, and lead in the sedimentary iron ores. The arsenic content of these ores in most cases is so high that it brings a very notable quantity of arsenic even into iron and steel, from which this element is difficult to eliminate by the usual technical processes of refining. Molybdenum is concentrated in oxidate sediments of manganese compounds.

One very interesting, and as yet unexplained, fact of the marine balances of minor constituents is that copper is present in sea water in relatively large amounts as compared with most other heavy metals. I do not know the cause for the exceptional concentration of copper as compared, *e.g.*, with the apparently almost complete elimination of nickel, and I think that continued investigations might be worth while.

A number of rare elements from sea water are concentrated in marine phosphate deposits. I may mention that one of our co-workers at Göttingen, Mr. Brundin from Lund, found large percentages of zinc in marine phosphates; and even cadmium, indium, and bismuth have recently been found to be concentrated in oceanic phosphate sediments.

Indium also is concentrated in sedimentary siderite rocks as well as in siderites of hydrothermal origin, probably because of the similarity of ionic radii between tervalent indium and bivalent iron. The presence of indium in siderites was noticed by Hartley and Ramage many years ago. Some data in connection with the occurrence of indium in siderite are appended :

Ionic radii, A.	In^{3+} 0·92.	Fe^{2+} 0·83.	Mn^{2+} 0·91.
	$InBO_3$.	$FeCO_3$.	$MnCO_3$.
Lattice constants { *a*, A.	5·84	5·75	5·84
Lattice constants { α	48° 10′	47° 52′	47° 46′

We see that in the third stage also of geochemical processes, *i.e.*, the cycle of sediment formation, the distribution of the chemical elements is regulated by the properties of their atoms and ions, the ionic potential being the most important property deciding the distribution in that stage.

As a next stage of geochemical evolution we may consider the processes of concentration due to the action of living organisms. Many such processes are well known to science, and Vernadsky, in particular, has called attention to their importance.

The elimination of phosphorus or of nitrogen compounds from sea water is the object of study by oceanographers and marine biologists, as shown in the admirable work of British biochemists among whom I may mention Dr. W. R. G. Atkins; and so also is the general circulation and balance of carbonic acid in sea water, which has been studied extensively by many investigators, lately especially by Dr. Wattenberg, of the Meteor Expedition.

The iodine cycle, the concentration of iodine in organisms, has been studied by von Fellenberg in Switzerland; the iodine metabolism of the marine bios has been investigated by Dr. G. Lunde and Dr. C. Closs in Norway, demonstrating in considerable detail the faculty of certain marine organisms to concentrate iodine up to several hundred thousand fold, as compared with sea water.

Other interesting phenomena are the accumulation of copper or vanadium by marine organisms.

If we study the single crystalline minerals of sedimentary rocks, we again recognise the importance of atomic and ionic radii in the distribution of rare elements between different minerals. One interesting feature is the accumulation of cobalt in the pyrites of shales, just as in those of hydrothermal origin.

Some very remarkable concentrations of rare elements are met with in the hydrocarbons, as well as in bituminous rocks; this applies to the accumulation of vanadium, molybdenum, and nickel, which doubtless form organometallic compounds and migrate together with the hydrocarbons. In collaboration with Professor K. Krejci-Graf, I am now engaged in a study of these elements in connection with bituminous substances.

The connection between vanadium, nickel, molybdenum, and natural hydrocarbons is the more interesting, for it is just these elements which are the most effective catalysts for

the industrial synthesis of hydrocarbons, and they may have been active in Nature by facilitating reactions between hydrogen sulphide and organic substances. Without doubt in these cases special atomic properties, especially valency forces, are controlling the association between these metals and the hydrocarbons, an association which has caused the formation of the famous Minas Ragras deposit of vanadium sulphide in Peru. The correlation of vanadium and asphaltites has recently been studied in much detail by G. Fester in Argentina.

In the phenomena of concentration and selective distribution of rare elements treated above, we have in a great many cases found clear and simple connections to be operative between special atomic and ionic properties and the processes of concentration. There is, however, one field of concentration of rare elements where such a simple connection with specific atomic properties is not so obvious—that is the concentration of rare elements in the ashes of certain coal deposits. About seven years ago I found the rare element germanium to be concentrated in certain coal ashes; * the maximum amount, more than 1%, has been found in the ash of certain British coal seams from the Hartley district. Our further study of the matter revealed that other rare elements also have been concentrated in just those types of coal which are rich in germanium. The following elements have been found to be concentrated in such coal ash : Li, Be, Sr, Ba, B, Sc, Y, La—Cp, Zr, Hf, V, Co, Ni, Mo, Rh, Pd, Pt, Cu, Zn, Ga, Ge, As, (Se ?), Ag, Cd, In, Sn, Sb, I, Au, Tl, Pb, Bi.

These observations agreed with older data on the occurrence of, *e.g.*, zinc, cadmium, lead, nickel, copper, molybdenum, tin, and lead in coal ash and flue dusts, and as the investigations were continued, nearly all rare elements were found concentrated in certain coal ashes. The following table summarises some of the results.

Rare Elements in Ashes of Coal (g. per ton).

Element.	Maximum.	Average of "rich" ashes.	Earth's crust.	Factor of enrichment. Maximum.	Factor of enrichment. Average.
B	3,000	600	3	1000	200
Ge	11,000	500	7	1600	70
As	8,000	500	5	1600	100
Bi	200	20	0·2	1000	100
Be	1,000	300	5	180	50
Co	1,500	300	40	35	8
Ni	8,000	700	100	80	7
Zn	10,000	200	40	250	5
Cd	50	5	0·5	100	10
Pb	1,000	100	16	60	6
Ag	5—10	2	0·1	50—100	20
Au	0·2—0·5	—	0·005	40—100	—
Pt	0·7	—	0·005	120	—
Li	500	—	65	8	—
Sc	400	60	5	80	3—12
Ga	400	100	15	27	7
Y	800	100	31	26	3
Zr	5,000	—	190	26	—
Mo	500	200	15	33	15
In	2	—	0·1	13	—
Sn	500	200	40	13	5
Tl	5	1	0·3	17	3

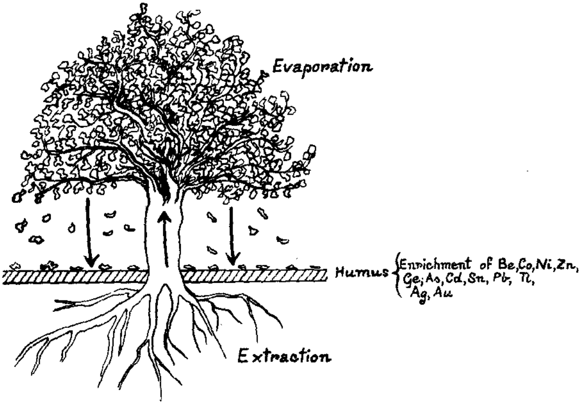
The most remarkable feature of these data seems to be that the concentration is operative on a great number of elements, belonging to the most diverse groups of the periodic system, with regard both to their chemical affinity properties and to their atomic radii and valency or ionic charge. Typical lithophile elements, such as beryllium and rare-earth

* Our first results concerning the enrichment of germanium in coal ash date from 1930; among the first specimens studied was a very rich coal from the collections of the Mineralogical Institute at Göttingen, labelled "*Coal from the Main Seam, Hartley, near Newcastle.*" Through the kindness of British colleagues we have been able to study also further samples from the same district. I may mention that the incineration of the coals has to be made in very thin layers, preferably after moistening with nitric acid, in order to avoid loss of volatile germanous compounds, such as germanous oxide and sulphide, from the ashes.

elements or zirconium and niobium, are being concentrated together with siderophile and chalcophile elements, such as precious metals, lead, bismuth, and arsenic. Typical cation elements such as lithium, and complex anions, such as those of boric acid, are concentrated.

Most interesting is the circumstance that the factor of enrichment is about the same in a great many cases, a coincidence which is the more remarkable in view of the extreme chemical diversity of the elements involved. One has to consider whether some simple process has been operative, a process not of a chemical but of a physical nature, which involves many elements jointly.

FIG. 3.



I think one could imagine some process which may be effective in that manner, a process connected with plant life, for instance in a forest. The soil solutions dissolve the inorganic constituents of the sub-soil according to their solubility, as we normally only have a small amount of solvent compared with the bulk of mineral matter. These solutions enter the plant organism through the roots of the plants, and at the place of strongest evaporation, especially in the leaves, the greater part of the mineral matter is deposited. The dead leaves accumulate at the surface of the ground, decaying into humic substances. The most soluble mineral constituents of the leaves and of their products of decay, such as carbonates and sulphates of lime, magnesium, sodium, and potassium, and humates of iron, are swept downwards by circulating rain water, and insoluble or sparingly soluble compounds are filtered off in the humus layer, perhaps in some cases being precipitated as organic complex compounds. By such processes many different chemical elements have been found to become concentrated in the uppermost humus layer of forest soils; we may illustrate this by data from a very old forest of beech and oak in Germany (Sababurg, north of Cassel).

Enrichment of Elements during Decay of Oak and Beech Humus (g. per ton).

	B_2O_3.	MnO.	NiO.	GeO_2.	As_2O_5.	Ag.	Au.
Mineral soil (sand)	7	400	20	5	—	—	—
Ash from fresh oak leaves	5,000—10,000	20,000*	50	5	—	—	—
Ash from oak humus............	200	2,400	100	70	—	1	—
Ash from beech humus	30	1,400	100	70	500	5	0·5

* Ash from fresh beech leaves; in leaves from the previous year, MnO = 7700 g.

Other elements concentrated in the humus are: Be, Co, Zn, Cd, Sn, Pb, and Tl.

We find in the humus ashes enrichment of many different elements, in many respects

analogous to the concentration of rare elements in coal ash. I consider it most likely that the concentration of rare elements in coal ash could have arisen in the same manner as the concentration in ashes from humus soil. The conclusion is that such " rich " coals may have been formed wholly or partly from fossil humus soils. Of course, biological processes also may, in some cases, be involved in the acts of concentration, especially with regard to some elements placed at the beginning of our table, elements which show the greatest factor of concentration, especially boron, an element which in many cases is strongly concentrated in the ashes of living plants.

For most of the elements, however, the process seems to be essentially an inorganic physical process. The function of the plants seems mainly to be that of a filtering and evaporating apparatus, which delivers its products to the uppermost stratum of the soil, where the products of evaporation again are partly dissolved, mainly as bicarbonates, and where the most insoluble compounds are filtered off from the more soluble ones, which re-enter the circulation in soil and plants.

Here we have a process of concentration, by means of fractional extraction by a kind of countercurrent leaching, evaporating, and redissolving device, which to a considerable extent is independent of special chemical properties of the elements involved and generally tends to concentrate rare elements relatively to the common ones. The end product of the process will be a sub-soil deprived of most of the rarer constituents, and an uppermost humus layer rich in rare elements. I think the common association of coal seams together with underlying refractory sands and clays deprived of soluble components may be indicative of the existence of such processes.

It would be worth while to investigate these processes also in present forest soils of wet and hot tropical regions. Even if a typical humus layer is not present in such soils, it might be important to compare the percentages of rarer elements in the sub-soil and in the surface layer. Biological observations on the sterile mud bottoms of some tropical forests might suggest the existence of such phenomena. Also the influence of rare soil constituents, such as zinc and arsenic, on the micro-flora of humus soils might be worth an investigation.

One question, which of course must be answered in connection with these phenomena, from a geochemical point of view, is why such processes of local concentration of rare elements by leaching and redeposition are not found more generally also in vein formation. The answer might be as follows. In order to make possible a leaching of compounds of rare elements corresponding, not to their percentages, but to their solubilities, the raw material must be present, not as the usual crystalline isomorphous mixtures, in which the rare elements are shielded against leaching actions, but as a finely disintegrated, preferably amorphous, material which is easily percolated by solutions. This condition generally obtains only in the zone of mineral weathering, not in compact crystalline rocks. Therefore, we find it as a soil phenomenon, not as a common geological process of deeper strata of the earth's crust.

Perhaps some of my audience may think that the subject of the last discussion is rather far removed from chemical mineralogy and chemical geology. However, some beautiful processes of mineral formation or even ore formation are connected with the same processes. The fine crystal needles of nickel monosulphide, millerite, often found in connection with coal seams, the cobalt nickel sulpho-spinel linnaeite, found in many British coal seams, and the arsenopyrites of coal are all connected with the same process of enrichment of rare elements. Moreover, one very important ore deposit may wholly or partly owe its existence to the erosion and redeposition of old enriched humus soils : that is the bituminous copper shale of Germany and Russia, in which we find associations of rare elements which have much in common with the element assemblages of humus soils and humus coals.

Of course, it is scarcely possible, within one single hour, to give an exhaustive report of the processes of element migration and element distribution involved in geology, mineralogy and even biology. However, I have attempted to give a sketch of our growing knowledge of geochemistry, of the principles governing the distribution of the chemical elements, and the application of these principles to some important stages of evolution of terrestrial matter.

I have tried to demonstrate four principal stages of geochemical evolution of matter.

The first stage represents the partition according to affinity properties, which govern the partition between ionic, semi-metallic, and metallic phases, besides eventually a vapour phase, having come into action during the very early history of the earth. The second stage during processes of crystallisation represents the sifting and sorting of elements by crystals, according to particle size, especially ionic size, the order of introduction into fitting crystal lattices being controlled according to ionic charges. In the third stage of geochemical evolution, represented principally by the formation of sedimentary rocks, the quotient between ionic charge and ionic radius, the ionic potential, is a most important principle, governing the distribution of elements in the sediments. The fourth stage, controlled by the activities of living organisms, again furnishes remarkable concentrations and assemblages of elements, in part governed by special chemical valency properties, and in part directed by dominatingly physical principles.

During the last year, new research facilities for geochemistry have been opened at the laboratories of the Geological Museum at the Royal Frederiks University at Oslo, in cooperation with the Royal Norwegian Ministry of Trade and Industry. I hope that the coming years may bring further advances in our knowledge concerning the distribution of the elements.

APPENDIX.

Publications on Geochemistry from the Mineralogical Institute of the University of Göttingen, 1930—1936.

Nachrichten von der Gesellschaft der Wissenschaften zu Göttingen, Math.-phys. Kl., Fachgruppe IV (Geologie u. Mineralogie).

V. M. Goldschmidt: Elemente u. Minerale pegmatitischer Gesteine, 1930, 370.
V. M. Goldschmidt: Ueber das Vorkommen des Germaniums in Steinkohlen und Steinkohlen-Produkten, 1930, 398.
V. M. Goldschmidt: Zur Kristallchemie des Germaniums, 1931, 184.
V. M. Goldschmidt and Cl. Peters: Zur Geochemie des Galliums, 1931, 165.
V. M. Goldschmidt and Cl. Peters: Zur Geochemie des Scandiums, 1931, 257.
V. M. Goldschmidt and Cl. Peters: Zur Geochemie des Berylliums, 1932, 360.
V. M. Goldschmidt and Cl. Peters: Zur Geochemie der Edelmetalle, 1932, 377.
V. M. Goldschmidt and Cl. Peters: Zur Geochemie des Bors, I und II, 1932, 402 and 528.
V. M. Goldschmidt and Cl. Peters: Zur Geochemie des Germaniums, 1933, 141.
V. M. Goldschmidt and Cl. Peters: Zur Kenntnis der Troilitknollen der Meteoriten, 1933, 278.
V. M. Goldschmidt and Cl. Peters: Ueber die Anreicherung seltener Elemente in Steinkohlen, 1933, 371.
V. M. Goldschmidt and Cl. Peters: Zur Geochemie des Arsens, 1934, 11.
V. M. Goldschmidt, Cl. Peters, H. Berman, and H. Hauptmann: Zur Geochemie der Alkalimetalle, 1933, 235.
V. M. Goldschmidt and H. Hauptmann: Isomorphie von Boraten u. Karbonaten, 1932, 53.
V. M. Goldschmidt and O. Hefter: Zur Geochemie des Selens, 1933, 245.
V. M. Goldschmidt and L. W. Strock: Zur Geochemie des Selens, II, 1935, 123.
V. M. Goldschmidt, H. Bauer, and H. Witte: Zur Geochemie der Alkalimetalle, II, 1934, 39.
E. Minami: Selen-Gehalte von europäischen und japanischen Tonschiefern, 1935, 143.
E. Minami: Gehalte an seltenen Erden in europäischen und japanischen Tonschiefern, 1935, 155.
L. W. Strock: Zur Geochemie des Lithiums, 1936, 171.
Th. Ernst and H. Hörmann: Bestimmung von Vanadium, Nickel und Molybdän im Meerwasser, 1936 205.

Zeitschrift für anorganische und allgemeine Chemie.

E. Thilo: Ueber die Resultate der Analysen zweier Kohlenaschen, 1934, **218**, 201.
H. Bauer: Quantitative Analyse schwer verdampfbarer Stoffe im Lichtbogen, untersucht am Lanthanoxyd, 1934, **221**, 209.

Industrial and Engineering Chemistry.

V. M. Goldschmidt: Rare Elements in Coal Ashes, 1935, **27**, 1100.

Chemie der Erde.

W. Noll: Geochemie des Strontiums, 1934, **8**, 507.
W. v. Engelhardt: Geochemie des Bariums, 1936, **10**, 187.

Fortschritte der Mineralogie.

V. M. Goldschmidt: Grundlagen der quantitativen Geochemie, 1933, **17**, 112.

V. M. Goldschmidt: Grundlagen der quantitativen Geochemie, II, 1935, **19**, 183.

Geologiska Föreningens i Stockholm Förhandlingar.

V. M. Goldschmidt: Drei Vorträge über Geochemie, 1934, **56**, 385.

Teknisk Ukeblad, Oslo.

V. M. Goldschmidt: Geokjemiske Forskningsarbeider i Göttingen, 1936, **83**, No. 11.

Die Naturwissenschaften.

V. M. Goldschmidt: Geochemische Verteilungsgesetze und kosmische Häufigkeit der Elemente, 1930, **18**, 999.

V. M. Goldschmidt: Geochemische Leit-Elemente, 1932, **20**, 947.

V. M. Goldschmidt, H. Hauptmann, and Cl. Peters: Ueber die Berücksichtigung seltener Elemente bei Gesteins-Analysen, 1933, **21**, 363.

Zeitschrift für physikalische Chemie.

V. M. Goldschmidt: Ueber das Vorkommen des Germaniums im Meteoriten von Cranbourne, 1930, *A*, **146**, 404.

Handwörterbuch der Naturwissenschaften, 2nd ed., Jena.

V. M. Goldschmidt: "Geochemie," 1933.

For a table of ionic radii, see V. M. Goldschmidt: "Kristallchemie," 1934.

Concerning the methods of quantitative spectrum analysis by means of the carbon arc, reference is given to articles by R. Mannkopff, Cl. Peters, H. Witte, H. Hörmann in *Zeitschrift für Physik* and to a summary by L. W. Strock, published by Adam Hilger, Ltd., 1936.

Numerous data from investigations made together with Dr. Bauer, Dr. Hörmann, and Dr. Witte on the geochemistry of various elements will be published in the near future, as well as the investigations jointly with Prof. K. Krejci-Graf on rare metals in bituminous substances.

ANNUAL GENERAL MEETING

The Ninety-Sixth Annual General Meeting was held at Burlington House on Thursday, March 18th, 1937, at 4 p.m., the President, Professor N. V. Sidgwick, C.B.E., D.Sc., F.R.S., occupying the Chair.

The notice convening the meeting was read.

The Report of Council for 1936 (see pp. 675-687) was presented and the Senior Honorary Secretary gave a brief survey of the principal developments of the work of the Society during the year. Attention was drawn to the fact that the Report was concerned with the affairs of the Society up to December 31st, 1936, and that future Reports would deal with matters for the previous calendar year.

The Treasurer, who was then called on by the President, dealt with the Accounts in some detail. He stated that in 1936 the deficit was £303, as against £1642 in 1935, and that the total income for this year showed an increase of £149 over the previous year. He referred to the decision of Council to transfer from Publications Fund to General Purposes Account the sum received (and invested) as Life Composition Fees since 1923, and to credit one-third of the amount received each year as Life Composition Fees to revenue.

On the expenditure side of the Accounts, the Treasurer stated that there had been slight increases in the cost of administration and of meetings; but the main item of expenditure, the contribution to the Publications Fund, was down by £64. The most important saving effected was in the contribution to the Library Fund (£666), due to subscriptions received from the Institute of Chemistry and the Society of Chemical Industry under the Agreement; also no contribution had been made towards the cost of the Collective Index. The *Journal* cost £65 less and the Abstracts £106 more than in 1935.

The Treasurer referred to the successful work of the Chemical Council in accomplishing reductions in the contracts for printing and paper, by which the Society would benefit in 1937, and in collecting funds which would become available for the support of publications.

Dr. Francis Carr, in moving the adoption of the Report of Council and Balance Sheets, referred to the important part played by the Chemical Society in promoting chemical science. He pointed out that the widening ramifications of chemistry called for ever-increasing work on the part of the President, Treasurer, and other Officers of the Society, and that though there had been a great increase in the number of British chemists, there had not been a corresponding increase in the membership of the Society. He welcomed the relief the Treasurer enjoyed through the prospect of external contributions being made towards the Library and publications; but emphasised the desirability of the complete independence which would result if the number of Fellows were commensurate with what was deserved of the Society. This was seconded by Professor J. C. Philip, and carried.

A Vote of Thanks to the Auditors, Dr. H. E. Cox, Dr. H. D. K. Drew, and Dr. G. Senter, proposed by the Treasurer and seconded by Dr. J. T. Hewitt, was carried. On the motion from the Chair, they were re-elected Auditors for the ensuing year.

A Vote of Thanks to the Treasurer, Honorary Secretaries, Council, and Committees for their services during the year, proposed by Professor W. E. Garner and seconded by Mr. F. P. Dunn, was passed unanimously and acknowledged by Sir Robert Robertson.

The report of the Scrutators on the ballot for the election of Ordinary Members of Council (Town and Country) was presented, and the following were declared as elected:

President: Professor F. G. Donnan.

Vice-Presidents, who have filled the office of President: Professor N. V. Sidgwick, Professor W. P. Wynne.

Vice-Presidents, who have not filled the office of President: Professor G. Barger, Professor J. C. Philip, Dr. R. H. Pickard.

Honorary Secretary: Dr. C. W. Davies.

Ordinary Members of Council (Town Members): Professor H. V. A. Briscoe, Mr. F. P. Dunn, Professor R. Robison, Dr. W. H. J. Vernon.

Ordinary Members of Council (Country Members): Dr. F. B. Kipping, Dr. E. H. Rodd.

A Vote of Thanks to the Scrutators (Dr. H. J. Emeléus and Dr. W. H. Patterson) was proposed by Professor R. Robison, seconded by Dr. F. B. Kipping, and carried.

The President then delivered his Address entitled: "Hybrid Molecules." At the conclusion of the Address, a Vote of Thanks to the President for his services in the Chair during his term of office and for his Address was proposed by Mr. W. A. S. Calder and seconded by Professor T. S. Moore. This was carried with acclamation, and in acknowledging the Vote of Thanks, the President referred to the valuable assistance he had received from the Treasurer and Honorary Secretaries and from the Assistant Secretary and members of his staff.

REPORT OF COUNCIL, 1936.

During the year much attention has been given to the improvement and extension of the services which the Society renders to its Fellows. The Publication Committee has considered the operation of the system for dealing with papers submitted for publication, and special Committees have been appointed to examine such varied questions as the status and responsibilities of Local Representatives, means for improving abstracts in Biochemistry, symbols for physico-chemical quantities, and ways and means of increasing the membership of the Society. Council has received and acted on the reports of some of these Committees and expects to receive reports from the others early in 1937. It is noteworthy that the suggestions which led to many of these aspects of the work of the Society being brought under review originated from Local Representatives or other Fellows of the Society in various parts of the country. The Council welcomes these evidences of the active interest which Fellows are taking in the progress of the Society, and wishes it to be known that careful consideration will always be given to constructive proposals for the improvement of any branch of the Society's activities.

Membership of the Society has remained practically stationary for a number of years, and the Council hopes that Fellows will take every opportunity of bringing the claims of the Society to the notice of those who are engaged in any branch of the profession of chemistry or who benefit directly or indirectly from the results of chemical research.

The work of the Chemical Council is leading to the establishment of closer relations with the Institute of Chemistry and the Society of Chemical Industry, and has already brought about some co-ordination of the services which the three Chartered bodies render to the science and profession of chemistry. Important developments in this direction may be expected in the future.

The Society has also co-operated with the Physiological Society, the Biochemical Society, the Physical Society, and the Faraday Society in examining certain matters of common interest referred to below, and the Council acknowledges the value of this co-operation.

In the previous Report an innovation was effected in that Fellowship Statistics were given to the 31st December, 1935, so as to conform with the Accounts. In future it is intended that the whole Report of Council shall refer to affairs for the calendar year. In the present Report all aspects of the work of the Society have been reviewed to the 31st December, 1936, but in the case of Meetings (section III and Appendix D) events already referred to in the previous Report have not been included.

I. FELLOWSHIP.

(1) *Honorary Fellows.*

The Council records with deep regret the death on the 17th September of Professor Henry Louis Le Chatelier, who was elected an Honorary Fellow of the Society on the 6th February, 1908. The condolences of the Council were conveyed to Madame Le Chatelier, and a Memorial Lecture will be delivered by Professor C. H. Desch in 1937.

(2) *Fellowship Statistics.*

The number of Fellows on the 31st December, 1935, was 3725. During the year, 205 Fellows were elected and 22 reinstated, the corresponding figures in 1935 being 228

and 21, respectively. The Society has lost 49 Fellows by death, 91 by resignation, and 66 by removal for non-payment of annual subscriptions, compared with 48, 38, and 66, respectively in 1935.

The number of Fellows on the 31st December, 1936, was 3746, showing a net increase of 21.

Note.—For purposes of comparison with the figures given in the last Report of Council, the resignations in 1935 should be increased by 63, making the number 101.

(3) *Birthday and New Year Honours.*

The congratulations of the Society were conveyed to the following Fellows, whose names appeared in the Birthday and New Year Honours:

Mr. William F. Donald	M.B.E.
Dr. C. Stanton Hicks	Kt.
Mr. Percy G. Lloyd	M.B.E.
Sir Harry McGowan	Baron
Professor Gilbert T. Morgan	Kt.
Mr. H. T. Tizard	K.C.B.

(4) *Fellows who have completed* 60 *and* 50 *years of Fellowship.*

Announcements have been made at Ordinary Scientific Meetings and published in the Proceedings of the congratulations of the Society that have been sent to those Fellows who during the year completed 60 years and 50 years of Fellowship.

(5) *List of Fellows.*

The List of Fellows was published in October, and can be obtained (price 1*s.*) from the Assistant Secretary.

(6) *Means of Increasing Membership of the Society.*

The Council appointed in June a Special Committee to consider ways and means of increasing the membership of the Society. It is expected that this Committee will present a report of its findings early in 1937.

II. PUBLICATIONS.

(1) *Journal.*

The *Journal* for 1936 contains 1862 pages (45 pages fewer than the *Journal* for 1935), and consists of 414 memoirs and 28 notes (1765 pages), 5 lectures (53 pages), the Presidential Address (5 pages), report of the Annual General Meeting (16 pages), and Obituary Notices (23 pages). The 414 memoirs comprise 128 dealing with General, Physical and Inorganic Chemistry and 286 dealing with Organic Chemistry.

During 1936, 466 papers were received; of these, 9 were declined.

In view of certain criticisms regarding the operation of the system for dealing with papers submitted for publication, Local Representatives and other Fellows in various parts of the country were invited to collect and forward the views of Fellows on the system. The replies showed that though the essential principles of the system were generally approved, some dissatisfaction existed regarding certain features of its operation. A number of proposals designed to remove a few definite grievances and to facilitate the smooth working of the system have been adopted. The refereeing and editing processes have been overhauled, and the Referee report forms amended accordingly.

In addition to this, the Council has decided to invite authors who publish frequent serial contributions on particular subjects to consider the possibility of holding over reports of the parts of an extensive investigation for publication at a suitable time, either as a single comprehensive paper, or as a group of papers arranged for continuous reading. Such a paper or group of papers could contain a single statement of the basic ideas of the whole investigation and could be made much more interesting to the general reader than is otherwise possible.

Other proposals for facilitating publication and for improving the *Journal* are under consideration.

At the request of the Chemical Council, the Council re-considered the question of allowing non-Fellows to publish papers occasionally in the *Journal*. The following statement on this matter now appears in " Notices to Authors of Papers " :

" A paper is not normally considered for publication in the *Journal* unless at least one of the authors is a Fellow of the Society, but in exceptional circumstances the Council is prepared to consider papers submitted by non-Fellows."

(2) *Abstracts.*

The Report of the Bureau of Chemical Abstracts for the year is reproduced in full as Appendix B to this Report.

British Chemical Abstracts " A " in Sections.

The Council decided, after consultation with the Bureau of Chemical Abstracts, that as from the beginning of 1937 British Chemical Abstracts " A " (Pure Chemistry) shall be issued in three sections: A., I., General, Physical, and Inorganic Chemistry; A., II., Organic Chemistry; and A., III., Biochemistry; and that this shall also apply to Abstracts printed on one side of the page. Each section will be separately paginated, and the Abstracts printed on both sides of the page will be issued in separate covers. One index will be issued for the whole of British Chemical Abstracts, " A " and " B," as heretofore.

Fellows have the privilege of receiving all three sections of Abstracts " A " and the general Index, should they so desire, but it is believed that many Fellows will take only one or two sections, and thus avoid the need for storing and binding other sections which they would seldom use.

Another innovation is that Fellows may now obtain Abstracts " A " printed on one side of the page *instead of* the ordinary issue, on payment of a small charge.

Additional copies of sections of Abstracts " A," printed on either one or both sides of the page, may be purchased separately at special rates.

Biochemistry Abstracts.

In June 1935, the attention of Council was directed to the steady increase in the number of abstracts in the Biochemistry section of British Chemical Abstracts " A," and a committee was appointed to consider the matter. It was decided that, as a temporary measure, the Bureau of Chemical Abstracts should be asked to effect a ten per cent. reduction in Biochemistry Abstracts in 1936; but that the matter should be referred to a Joint Committee of representatives of the Chemical Society, the Biochemical Society, the Physiological Society, and " Nutrition Abstracts and Reviews," with the Editor of British Chemical Abstracts, for consideration and report. This Joint Committee was instituted in November 1935, but representatives of " Nutrition Abstracts and Reviews " afterwards withdrew. In its report issued in November 1936, the Joint Committee recommended a definite scheme for the future publication of abstracts in biochemistry and physiology. The proposals are still under consideration.

(3) *Annual Reports.*

Volume XXXII of the Annual Reports for 1935 was published in April, and included, in addition to the usual reports, a biennial report on Crystallography for 1934 and 1935. It contained 485 pages compared with 408 pages in the previous volume.

III. MEETINGS.

(1) *Scientific Meetings.*

The Society has held 14 meetings in London during the period March to December. These included 3 Lectures, 2 organised Discussions and 9 Ordinary Scientific Meetings at which 28 papers were read and discussed.

In arranging the organised Discussions it is now the practice for the opener to suggest

the names of certain Fellows who should be specially invited to contribute, and thus ensure that attention is given to various aspects of the subject chosen. Contributions from other Fellows desiring to take part in the discussion are, of course, always welcomed.

Eighteen meetings which were held outside London, included 16 lectures, and 2 meetings for the reading and discussion of papers. Fellows were also invited to attend the Bedson Lectures at Newcastle-on-Tyne.

A complete list of lectures and discussions is given in Appendix D to this report.

(2) *Anniversary Meetings.*

A report of the Anniversary Meetings held in Bristol in April 1936 appeared in the *Journal* and *Proceedings* for that month. The thanks of the Council were conveyed to the Chancellor, Council and Senate of the University of Bristol for hospitality; to the Director of the Agricultural Research Station, the National Smelting Co., Ltd., and Messrs. J. S. Fry & Sons, Ltd., for the visits; and to the Officers and Members of the Reception Committee for their valuable services in arranging the meetings.

IV. LIBRARY.

(1) *Management.*

In accordance with the terms of the Agreement entered into between the Chemical Society, the Institute of Chemistry, and the Society of Chemical Industry in the formation of the Chemical Council, the management of the Library has been delegated by the Council of the Chemical Society to a Joint Library Committee consisting of representatives nominated by the Councils of the three constituent bodies and by other organisations contributing to its maintenance.

The constitution of this Committee is as follows :

Chemical Society (14) : Prof. H. Bassett, Dr. O. L. Brady, Prof. J. W. Cook, Dr. C. H. Desch, Mr. M. B. Donald, Prof. A. C. G. Egerton, Dr. H. J. Emeléus, Prof. G. I. Finch, Prof. C. R. Harington, Dr. T. A. Henry, Dr. E. W. McClelland, Dr. W. H. Mills, Dr. E. E. Turner, and Dr. J. C. Withers.
Institute of Chemistry (4) : Prof. H. V. A. Briscoe, Mr. H. W. Cremer, Dr. J. J. Fox, and Dr. E. Vanstone.
Society of Chemical Industry (3) : Dr. J. B. Firth, Mr. A. McCulloch, and Prof. H. Raistrick.
Association of British Chemical Manufacturers : Sir Robert Mond.
Biochemical Society : Dr. P. Haas.
Faraday Society : Prof. J. R. Partington.
Institute of Brewing : Mr. H. W. Harman.
Society of Dyers and Colourists : Dr. C. Dorée.
Society of Public Analysts : Dr. C. Ainsworth Mitchell.

The Committee has elected Dr. O. L. Brady as its Chairman; and the Librarian acts as Secretary. Some adjustment was required to meet the new conditions resulting from the agreement and a sub-committee has been set up to revise the Library Rules and to consider general procedure. The former task has been completed, and the new rules will come into operation shortly when final approval has been given by the Chemical Council. A sub-committee has also been appointed to consider ways of meeting the urgent need for increased Library accommodation.

The Report of the Joint Library Committee is printed as Appendix C to this Report.

V. OTHER ACTIVITIES.

(1) *Grants for Research.*

In December applications for grants for research amounting to £908 were received from 86 Fellows. Grants amounting to £622 were allotted.

(2) *Decoration of Premises.*

The Council decided to re-decorate the apartments of the Society. The cost of this, amounting to £309 3*s*. 6*d*., has been met out of the Spencer Bequest Account. Decorations were last carried out in 1923.

VI. ADMINISTRATION.

(1) *Council.*

Secretaryship.

In June the Council received with much regret the resignation of Professor J. M. Gulland from the Office of Honorary Secretary on his appointment to the Chair of Chemistry at University College, Nottingham, and recorded its appreciation of the valuable services he rendered to the Society during his period of office from 1933 to 1936. Dr. C. W. Davies was appointed to fill the vacancy until the next Annual General Meeting in March, 1937.

Vacancy on Council.

Professor R. Robison was appointed an Ordinary Member of Council until the next Annual General Meeting to fill the vacancy caused by the election of Professor J. W. Cook as Honorary Secretary.

Service on Council of Vice-Presidents who have filled the office of President :—

Consideration has been given to the operation of Bye-Law VIII, which regulates the conditions of Service on Council of Vice-Presidents who have filled the office of President, and Council has decided to recommend to Fellows an amendment of this Bye-Law to remedy certain defects in its operation.

(2) *Local Representatives.*

During the year, the Council has accepted with much regret the resignation of the following Local Representatives : Prof. F. G. Soper (North Wales), Dr. A. Lauder (Edinburgh), Prof. W. H. Lewis (Exeter), and Dr. F. Fairbrother (Manchester), and has expressed its high appreciation of their valuable services. Dr. A. E. Bradfield, Dr. J. A. V. Butler, Prof. H. T. S. Britton, and Dr. G. N. Burkhardt were appointed to fill the respective vacant places.

A meeting of Local Representatives was held at the University of Bristol on the 17th April. Various suggestions put forward at this meeting were referred by Council to a committee composed of Local Representatives and the Officers. On the recommendation of this Committee it was decided—

(*a*) That the formation of Local Committees should be encouraged wherever desirable.
(*b*) That when a Committee is formed, the Local Representative should be the principal executive Officer.
(*c*) That opportunity should be given for the Committees to consider from time to time matters affecting the interests of the Society, and that the findings of the Committees should be communicated to the Council by the Local Representatives.
(*d*) That the Council should make an annual grant of not exceeding £5 to each area towards the expenses involved in the organisation of meetings.
(*e*) That Local Representatives should be appointed by the Council after consultation with the Local Committees, or with the Local Representative and Fellows in the area if a Committee has not been formed.
(*f*) That each appointment should be for a period of three years, and that Local Representatives should be eligible for re-appointment for one further period of three years. In the case of the present Local Representatives, appointment should date as from the Annual General Meeting on the 16th April, 1936.

VII. FINANCE.

General Purposes Account.

Expenditure has exceeded income by £303; in 1935 the adverse balance was £1642. The reduction of £1339 in the amount of the deficit is due mainly to a decrease of £666 in the amount contributed by the Society to the Library Fund. Also, in 1935 the sum of

£488 was allocated towards the cost of the Decennial Index, whilst this year this expenditure did not arise. Life Composition Fees show an increase of £131 due to one-third of these being taken as current income.

Publications Fund.

Income. Proceeds from the sale of publications were down by £14. Donations increased by £264.

Expenditure. The cost of the Journal is less by £66, Abstracts are up by £106 and Annual Reports by £112.

Life Composition Fees.

The Council decided that stock to the market value of £1863, representing the investment of £1451 2*s*. 11*d*. received on account of Life Composition Fees since 1923 should be transferred in the Balance Sheets from Publications Fund Account to General Purposes Account; that as from the 1st January, 1936, two-thirds of the Life Composition Fees should be capitalised and one-third treated as current income, and that this ruling should apply to Life Composition Fees amounting to £123 17*s*. 1*d*. received between June 1934 and December 1935, which had not yet been invested.

Donations.

The following donations have been received :

£700 from the Government Publications Grant (through the Royal Society),
£500 from Imperial Chemical Industries, Ltd.

The Council records its cordial thanks for these very welcome contributions to its funds.

Herbert Spencer Bequest.

The Society has received a bequest of £1241 under the will of the late Herbert Spencer.

Contributions to the Publications Fund.

The Council again expresses its appreciation of the generous assistance rendered by those Fellows who continue to subscribe annually towards the cost of the Society's publications.

Library Fund.

In accordance with the agreement constituting the Chemical Council, the three constituent bodies commenced to contribute to the cost of maintenance of the Library in proportion to their membership as from the 1st January, 1936. The amounts received under this scheme for 1936 were : £646 10*s*. from the Institute of Chemistry, £448 from the Society of Chemical Industry, and £382 19*s*. 10*d*, from the Chemical Society. In addition, £221 5*s*. was received from other contributing bodies. The Chemical Society has spent £820 0*s*. 9*d*. on the purchase of furniture, books, periodicals and binding, and has provided 97 copies of the Journal and 36 copies of the Abstracts "A" for exchange with other Journals.

VIII. RELATIONS WITH OTHER BODIES.

(1) *The Chemical Council.*

In the last report of Council reference was made to the formation and constitution of the Chemical Council.

During the year the Chemical Council has played an increasingly important part in co-ordinating the activities of the three constituent bodies—the Chemical Society, the Institute of Chemistry, and the Society of Chemical Industry. The establishment of the Joint Library Committee, and the operation of the agreement regarding contributions towards the cost of maintenance of the Chemical Society's Library are referred to in section IV of this Report. The first Annual Report of the Chemical Council is reproduced in full in Appendix A.

(2) *The Physiological Society and the Biochemical Society.*

See section II (2) of this Report.

(3) *The Physical Society and the Faraday Society.*

Arising out of the decision of the Chemical Society to revise the list of symbols authorised for use in its Journal, a Joint Committee of the Chemical Society, the Faraday Society, and the Physical Society was set up to secure a wider measure of agreement between chemists and physicists on the use of symbols for thermodynamical quantities. The scope of the work of the Joint Committee was afterwards extended to include symbols for other quantities of interest to both chemists and physicists. It is expected that the Joint Committee will present a final report early in 1937.

(4) *Representatives of the Society on other bodies.*

Association of British Chemical Manufacturers:
Committee *re* Patents and Designs Act: Prof. W. A. Bone.
Bristol University Court:
Prof. F. G. Donnan.
British National Committee for Chemistry:
President, Treasurer, and Senior Secretary.
British Standards Institution:
Council of Chemical Division: Dr. J. J. Fox.
Committees:
Specifications for Materials and Plant used in Electroplating: Dr. U. R. Evans.
Standardisation of Scientific Glassware: Dr. J. J. Fox and Dr. E. B. Hughes.
Standards for use in Dairying Chemistry: Mr. A. L. Bacharach.
Chemical Symbols and Abbreviations: Dr. A. D. Mitchell.
Bureau of Chemical Abstracts:
Mr. F. P. Dunn, Mr. A. J. Greenaway, Dr. J. T. Hewitt, and the Senior Secretary, with the Treasurer *ex-officio*.
Chemical Council:
Prof. N. V. Sidgwick, Prof. I. M. Heilbron, and Sir Gilbert Morgan.
City and Guilds of London Institute:
The President.
Faraday Society:
Colloid Committee: Prof. R. Whytlaw-Gray.
Home Office:
Air Raid Precautions Department: Mr. J. Davidson Pratt.
Joint Library Committee: (see IV).
Joint Committee on Biochemistry Abstracts:
Prof. J. M. Gulland and Prof. R. Robinson.
Joint Committee on Thermodynamical Symbols:
Dr. H. J. T. Ellingham, Prof. G. I. Finch, Prof. C. N. Hinshelwood, and Prof. E. K. Rideal.
Lawes Agricultural Trust:
Committee of Management: Prof. H. E. Armstrong.
Royal Microscopical Society:
Standardisation of Biological Stains: Prof. F. M. Rowe.

(5) *Representatives of the Society at Public Functions.*

University of London Centenary Celebrations (29th June to 3rd July).	The President.
American Academy of Political and Social Science, 40th Annual General Meeting, Philadelphia (24th and 25th April).	Prof. W. D. Bancroft, Col. M. T. Bogert, and Prof. H. J. M. Creighton.
National Conference of Roumanian Chemists (Constanta, 21st May).	Sir Robert Robertson.

IX. ACKNOWLEDGMENTS.

The Council expresses its cordial thanks to the many Fellows who have served the Society in various ways during the year, including Members of Committees, Referees of papers submitted for publication, Contributors to the Annual Reports, Local Representatives, and those who have given Lectures and opened Discussions.

The thanks of the Council have been conveyed to Mr. A. Bracher, Dr. J. N. Goldsmith, Miss T. M. Holmes, and to the Institute of Brewing, the Pontefract Public Library and the Royal Photographic Society for presenting volumes of the Society's publications; also to Dr. T. Seligman for a copy of the Ludwig Mond Memorial Medal in nickel and to the Wellcome Foundation, Ltd., for a replica of the medal struck to commemorate the services rendered to medicine and pharmacy by Dr. F. B. Power.

APPENDIX A.

FIRST ANNUAL REPORT OF THE CHEMICAL COUNCIL.

2nd December, 1936.

Constitution.—The Chemical Council was formed under a Deed of Agreement, to be in operation for seven years, between the Chemical Society, the Institute of Chemistry, and the Society of Chemical Industry—dated 1st July, 1935—for the administration of a fund for the co-ordination of scientific and technical publications, the publication of new discoveries in chemical science and their applications to the arts and manufactures, the promotion of research, the maintenance of a library for research and education purposes, and the provision and equipment of a suitable building or buildings for all or any of the purposes aforesaid.

The Council consists of twelve members, of whom three were nominated by each of the Councils of the Constituent Bodies, and three, as representatives of industry, co-opted (in the first instance) on the nomination of the Association of British Chemical Manufacturers.

The original Council was as follows:

Representing the Chemical Society:
Prof. I. M. Heilbron, D.S.O., D.Sc., F.R.S.
Prof. (now Sir) Gilbert T. Morgan, O.B.E., LL.D., D.Sc., F.R.S.
Prof. N. V. Sidgwick, C.B.E., M.A., Sc.D., F.R.S.

Representing the Institute of Chemistry:
F. G. Edmed, O.B.E., B.Sc., A.R.C.S., F.I.C.
Patrick H. Kirkaldy, F.I.C.
Prof. J. F. Thorpe, C.B.E., D.Sc., F.R.S.

Representing the Society of Chemical Industry:
L. H. Lampitt, D.Sc., F.I.C.
Robert H. Pickard, D.Sc., F.R.S.
J. Arthur Reavell, M.I.Chem.E., M.I.Mech.E.

Nominated by the Association of British Chemical Manufacturers:
A. E. Dunstan, D.Sc., F.I.C.
J. Davidson Pratt, O.B.E., M.A., B.Sc., F.I.C.
(The late) Wm. Rintoul, O.B.E., F.I.C.

Dr. Robert H. Pickard was appointed Chairman; Mr. J. Davidson Pratt, Vice-Chairman; and Professor Jocelyn F. Thorpe, Honorary Treasurer.

These Officers have been re-appointed for the ensuing year.

The Council records with deep regret the death of Mr. William Rintoul, in whose place Dr. R. E. Slade, M.C., F.I.C., has been co-opted.

The Council also regrets that, for reasons of health, Mr. Patrick H. Kirkaldy has recently been obliged to tender his resignation from the Council. The Council of the Institute of Chemistry has appointed Mr. W. A. S. Calder, F.I.C., in the place of Mr. Kirkaldy.

The Chemical Council has held twelve meetings.

Policy.—The Council, having appointed Officers and having framed Standing Orders for the conduct of its business, proceeded to determine its policy.

The Council aims at promoting co-operation between the three Chartered Chemical Organisations, with a view to effecting economies in administration and in publications,

in furthering the science of chemistry for the public good, in extending the publication of new knowledge and abstracts, and in the maintenance of the Chemical Library.

For these objects the Council is endeavouring to raise a fund, and looks for the sympathetic and active support of all industries which employ chemists, and of universities and institutions, as well as of chemists themselves. All are urged to support the Council and the societies in order that they may be in a position to provide the publications, library and premises necessary for the furtherance of the science, and that British chemistry may be placed on a sound foundation.

Library.—The Council has appointed a Committee for Library Organisation which has determined the amounts to be contributed by each of the Constituent Bodies to the maintenance of the Library of the Chemical Society, and, in consultation with the Council of the Chemical Society, has determined the composition of the Joint Library Committee, on which the three Constituent Bodies and other contributing societies are represented, the Chairman being appointed by the Joint Library Committee.

Publications.—The Council has appointed a Publications Committee which has investigated the cost of production of the publications of the Constituent Bodies, has obtained estimates for printing and paper, and, as a result, hopes to show that economies may be effected in production, and, in due course, in distribution. Mr. F. P. Dunn has kindly acted as Chairman.

Finance.—An Appeal Committee was appointed to prepare an appeal addressed to those who appreciate the value of chemistry in its practical applications to industry and commerce.

Before issuing the appeal, however, the Council deemed it advisable to secure a list of preliminary contributions and promises, and was very fortunate in obtaining a generous promise of £9,000 from Sir Robert Mond.

The Honorary Treasurer, Professor Thorpe, then addressed personal letters to many members of the Constituent Bodies, with the result that a sum of £5,640 has been promised from this source.

The appeal pamphlet was issued in June to a large number of industrial concerns and other organisations who were thought likely to take advantage of an opportunity of recognising the importance of science and the benefits to be derived from the encouragement of research, with the result that the Council at present has in view contributions and promises from this source amounting to £4,148. It is understood that several important companies have the matter under consideration.

On the winding-up of the Association of Scientific and Technical Institutions, a further sum of £2,128 was transferred to the funds of the Council.

The contributions promised to date, together with Income Tax recoverable under Deeds of Covenant, amount to an estimated total of £23,410 4*s.* 8*d.*, of which a sum of £8,712 13*s.* 1*d.* has actually been received.

The expenses to date amount to £147 7*s.* 2*d.*

Audited Accounts to 30th September and a Summary to 4th December are attached.

RECEIPTS AND PAYMENTS ACCOUNT FOR THE FIFTEEN MONTHS FROM 1ST JULY, 1935, TO 30TH SEPTEMBER, 1936.

RECEIPTS.

Dr.

	£ s. d.	£ s. d.	£ s. d.
To *Contributions:*			
Under Deeds of Covenant ...	539 6 11		
Less Income Tax	127 10 11		
		411 16 0	
Not under Deeds of Covenant..........		93 5 3	
		505 1 3	
Donations		6153 3 7	
			6658 4 10
Deposit Interest..............			20 14 2
			£6678 19 0

PAYMENTS.

Cr.

	£ s. d.	£ s. d.
By Printing and Stationery	85 18 1	
,, Postages	35 10 0	
,, Bank Charges	4 12 5	
,, Stamp Duty on Deeds of Covenant	18 9 6	
,, Sundry Expenses	2 17 2	
		147 7 2
,, *Balance at Bankers:*		
Deposit Account	6314 1 1	
Current Account	212 11 0	
	6526 12 1	
Cash in Hand............	4 19 9	
		6531 11 10
		£6678 19 0

INCOME AND EXPENDITURE ACCOUNT FOR THE FIFTEEN MONTHS FROM 1st JULY, 1935, TO 30th SEPTEMBER, 1936.

EXPENDITURE.

	£	s.	d.	£	s.	d.
To Printing and Stationery	85	18	1			
,, Postages	35	10	0			
,, Stamp Duty on Deeds of Covenant	18	9	6			
,, Bank Charges	4	12	5			
,, Sundry Expenses..............	2	17	2			
				147	7	2
,, *Balance:* Excess of Income over Expenditure for fifteen months				6659	2	9
				£6806	9	11

INCOME.

	£	s.	d.	£	s.	d.
By *Contributions:*						
Under Deed of Covenant.....................	539	6	11			
Not under Deed	93	5	3			
Donations	6153	3	7			
				6785	15	9
Deposit Interest				20	14	2
				£6806	9	11

23rd October, 1936.

(*Signed*) J. Y. FINLAY, C.A.
(J. Y. Finlay & Co., Ltd.)

Premises.—Preliminary consideration has been given to the question of premises. The offices at present occupied by the Society of Chemical Industry are very inadequate, and the lease thereof will expire early in 1937. There is now no available accommodation at Burlington House for the increasing Library of the Chemical Society.

The Registrar and Secretary of the Institute of Chemistry has acted as Honorary Secretary, and the Council has had the advantage of the services of the staff of the Institute.

APPENDIX B.

REPORT OF THE BUREAU OF CHEMICAL ABSTRACTS FOR 1936.

Three Meetings of the Bureau were held during the year.

Abstracts.—The total number of abstracts published during 1936 was 34,321 as compared with 31,349 in 1935, an increase of 2,972. The appended table shows the number of abstracts and pages printed in each quarter, as well as the average length, the figures for 1935 being included for comparison.

	Abstracts A.				Abstracts B.			
	1935.		1936.		1935.		1936.	
	No. of Abs.	Pages.	No. of Abs.	Pages.	No. of Abs.	Pages.	No. of Abs.	Pages.
1st quarter	4,630	422	4,464	396	3,326	272	3,840	286
2nd ,, ...	4,114	376	4,243	372	3,846	304	4,026	288
3rd ,, ...	4,056	384	4,396	398	3,596	288	4,386	320
4th ,, ...	3,855	370	4,295	406	3,926	304	4,671	344
	16,655	1,552	17,398	1,572	14,694	1,168	16,923	1,238
Average length per abstract...........	0·19 Col.		0·18 Col.		0·16 Col.		0·15 Col.	

The 17,398 "A" Abstracts comprised 7672 in General, Physical, and Inorganic Chemistry, 564 in Geochemistry, 3156 in Organic Chemistry, and 6006 in Biochemistry. The corresponding figures for 1935 were 7601, 519, 2617, and 5918.

Of the 16,923 "B" Abstracts, 8771 were from journal literature and 8152 were abstracts of Patents (in 1935, 8351 and 6342 respectively).

The number of pages of Biochemistry abstracts printed in 1936 was 431, compared with 477 in 1935. This reduction of approximately 10 per cent. was effected at the request of the Council of the Chemical Society. It will be observed that, in spite of this reduction in

number of pages, the number of Biochemistry abstracts printed shows an increase of 88 over 1935.

The most noteworthy changes in numbers of abstracts have been increases of 539 (20 per cent.) in Organic Chemistry and 1809 (28 per cent.) in the abstract of Patents.

At the request of the respective Councils, steps have been taken to issue the "A" Abstracts in three separate sections, A., I, General, Physical, and Inorganic Chemistry, and Geochemistry; A., II, Organic Chemistry; and A., III, Biochemistry; each with separate pagination and monthly author index, and also to publish the "B" Abstracts monthly instead of issuing each set fortnightly divided in two weekly issues. This latter change has been rendered possible by the decision of the Society of Chemical Industry to issue its Transactions and Abstracts separately from "Chemistry and Industry."

Editorial Staff.—No changes have taken place during the year, but it may be recorded that the arrangements for editing the Biochemistry Abstracts are operating very satisfactorily.

Annual Index.—The joint Annual Index to the Abstracts for 1935 covered 754 pages, an increase of 62 pages over the 692 of the 1934 Index. The cost of printing the Index was £1445 19*s.* 9*d.* and of the paper £290 8*s.* 3*d.* (corresponding figures for the 1934 Index were £1343 16*s.* 0*d.* and £259 13*s.* 7*d.*). The total number of entries in the Index were 105,850 compared with 97,050 in 1934.

The Bureau is glad to be able to record that the measures adopted last year for speeding up the publication of the Index resulted in the volume being issued at the end of March, instead of during May as in the previous year.

Decennial Index. It was reported that last year 809 copies of the Decennial Index had been sold up to the end of 1935. Sales of 50 copies during 1936 bring the total up to 859.

In accordance with the arrangements made last year for allocating net proceeds of sales of the Index, the sum of £115 has been forwarded to each of the two Societies during the year.

Indexing Arrangements. The existing arrangements for indexing the abstracts have been carefully reviewed by the Bureau during the year, and a report has been presented to the two Societies recommending that a permanent assistant be appointed early in 1937, and asking that early consideration be given to the question of providing premises for the indexing department.

APPENDIX C.

REPORT OF THE JOINT LIBRARY COMMITTEE FOR 1936.

Excluding the evenings on which meetings of the Chemical Society were held, there were 8917 attendances during the year, as compared with 8156 in 1935. Of these 5377 were made by Fellows of the Chemical Society, and 3540 by Members of Contributing Societies, as against 5128 and 3028 in 1935.

One person recommended by the Academic Assistance Council has availed himself of the privilege of reading in the Library.

The number of books borrowed was 5594, against 5509 in the previous year; of these 1650 were issued by post, compared with 1378 in the preceding year.

The Library telephone facilities are still extensively used, and the incoming calls included 937 enquiries which necessitated reference to books in the Library, as against 852 the previous year.

The additions to the Library comprise :

257 books, of which 71 were presented; 734 volumes of periodicals and 224 pamphlets; as against 203 books, 662 volumes of periodicals and 233 pamphlets last year.

Analysis.

	Attendances.	Books borrowed.	Books added.	Volumes of periodicals.	Pamphlets
1936	8917	5594	257	734	224
1935	8156	5509	203	662	233

The total number of volumes added during the year was 991. The Library now contains 40,666 volumes, consisting of 12,277 books and 28,389 bound volumes of periodicals.

APPENDIX D.

LECTURES AND DISCUSSIONS.

Lectures held in London.

28th May, Fifth Pedler Lecture, entitled " Synthesis in Biochemistry," by Professor R. Robinson; 29th October, on " Mediaeval Pigments and Mediums used in Painting," by Professor A. P. Laurie; 10th December, Sixth Liversidge Lecture, entitled " Study of Transmutation in the Chemical Laboratory," by Professor F. Paneth.

Discussions held in London.

19th March, Joint Discussion with the Biochemical Society on " The Chemistry and Biochemistry of Lipoids "; 19th November, on " Mesomerism in Organic Chemistry," opened by Professor C. K. Ingold.

Lectures held outside London.

Birmingham. At the University, Edgbaston : 2nd November, on " Sterols, Sex Hormones and Carcinogenic Hydrocarbons," by Professor J. W. Cook; 7th December, on " Infra-Red Spectra and Chemical Constitution," by Dr. J. J. Fox.

Bristol. At the H. H. Wills Physics Laboratory : 17th April, Hantzsch Memorial Lecture, by Professor T. S. Moore.

Edinburgh. At the University : 10th November, on " Photodichroism and Related Phenomena," by Professor F. Weigert; 8th December, on " Recent Researches on Hormones," by Professor G. Barger.

Exeter. At the University College: 28th October, on " Electrometric Methods of Analysis and Investigation," by Professor H. T. S. Britton (held under the auspices of the Institute of Chemistry).

Leeds. At the University : 26th November, on " The Biological Breakdown of Carbohydrates," by Dr. H. A. Krebs.

Liverpool. At the University : 30th October, on " Electron Diffraction and Surface Structure," by Professor G. Ingle Finch.

Manchester. At the Constitutional Club : 2nd October (joint meeting with the Manchester Section of the Society of Chemical Industry) on " Synthesis of Aliphatic Acids under High Pressure," by Dr. D. V. N. Hardy; 24th November (joint meeting with the Manchester Section of the Society of Chemical Industry and the Manchester University Chemical Society) on " Chemical Detection of Artificially Produced Elements," by Professor F. Paneth.

Newcastle and Durham. Bedson Lectures at Armstrong College : 8th May, on " The Chemical Properties of Metals," by Professor C. H. Desch; 20th November, on " Chemistry of Nutrition," by Professor J. C. Drummond.

North Wales. At University College, Bangor (joint meetings with the University College Chemical Society): 30th October, on "The Biochemistry of Waxes," by Professor A. C. Chibnall.

Nottingham. At University College, University Park: 13th November (Joint meeting with Nottingham University College Physical and Chemical Society), on "Resonance in Organic Chemistry," by Professor N. V. Sidgwick. At University College, Shakespeare Street, 18th December (joint meeting with the Nottingham Section of the Society of Chemical Industry) on "Electrochemical Combustion of Fuel," by Dr. H. J. T. Ellingham.

Sheffield. At the University: 13th March, on "Carbohydrates," by Professor W. N. Haworth; 4th December, on "Molecular Structure of Strychnine," by Professor R. Robinson.

South Wales. At University College, Swansea (Joint Meetings with University College of Swansea Chemical Society): 30th October, on "Lipochrome Pigments in Plants and Animals," by Professor I. M. Heilbron.

INCOME AND EXPENDITURE GENERAL PURPOSES ACCOUNT FOR THE YEAR ENDED 31ST DECEMBER, 1936.

Income.

1935 £ s. d.	1935 £ s. d.	Income.	1936 £ s. d.	1936 £ s. d.
	75 0 0	To Life Composition Fees (£404 7s. 1d.), one-third as Income		134 15 8
		,, Annual Subscriptions:		
888 3 0		Received in advance, on account of 1936 during 1936 ...	916 7 6	
7657 10 0		,, ,, ,, ,, 1935 ...	7677 8 6	
369 4 3		,, ,, ,, ,, 1934 and	345 0 0	
20 0 0		,, ,, ,, previous years	14 0 0	
8934 17 3			8952 16 0	
350 0 0		*Less* amount included in last year's Income, being valuation of Arrears as per last Balance Sheet	350 0 0	
8584 17 3			8602 16 0	
350 0 0		*Add* Arrears at date: £467 14s. 0d. Estimated to realise as per Balance Sheet ...	520 0 0	
	8934 17 3			8922 16 0
	796 6 4	,, Dividends on Investments		833 17 5
	226 15 6	,, Income Tax recovered		224 18 4
	14 18 2	,, Interest on Deposit		13 12 11
	5 0 0	,, Donation		—
	64 9 6	,, Miscellaneous Receipts		60 18 11
	1642 0 1	,, Excess of Expenditure over Income carried to Balance Sheet		302 19 10
	£11,759 6 10			£10,493 19 1

Expenditure.

1935 £ s. d.	1935 £ s. d.	Expenditure.	1936 £ s. d.	1936 £ s. d.
		By Administration Expenses:		
1978 6 3		Office Salaries and Wages	1993 13 10	
236 16 8		Superannuation	226 7 6	
214 2 8		House Expenses, etc. (proportion)	284 4 11	
52 10 0		Accountants' Charges	52 10 0	
279 15 1		Miscellaneous Printing and Stationery (proportion)	278 9 7	
167 8 3		Postages	183 3 8	
62 12 0		Miscellaneous	51 6 7	
	2991 10 11			3069 15 1
	163 2 10	,, Expenses of Meetings		212 9 4
		,, Donations:		
	5 5 0	British Standards Institution		5 5 0
	5996 0 4	,, Contribution to Publications Fund		5841 19 1
	75 0 0	,, Transfer to ditto (Life Composition Fees) ...		—
	1869 10 4	,, Contribution to Library Fund		1203 0 7
	74 16 5	,, Transfer to Staff Pensions Fund		77 12 4
	488 2 11	,, Transfer to Special Publications Fund for Collective Index, 1923–32		—
	78 15 5	,, Expenses of Local Representatives		83 17 8
	42 17 10	,, Expenses of formation of the Chemical Council		—
	64 5 0	,, Legal Expenses in connection with alterations to the Bye-Laws		—
	£11,759 6 10			£10,493 19 1

THE HERBERT SPENCER BEQUEST.

Income.	1936 £ s. d.
To Amount received from the Trustees	1241 0 0
	£1241 0 0

Expenditure.	1936 £ s. d.
By Expenditure on repairs to premises	309 3 6
,, Balance unexpended	931 16 6
	£1241 0 0

PUBLICATIONS FUND.

Income.

1935 £ s. d.	1935 £ s. d.	Income.	1936 £ s. d.	1936 £ s. d.
		To Publication Sales (including back numbers):—		
2479 19 2		Journals and Proceedings	2502 11 4	
1891 15 7		Abstracts	1878 10 8	
29 7 6		Collective Index, Vols. I–VI	23 15 0	
45 0 0		Do. 1923–32	115 0 0	
853 5 0		Annual Reports on Progress of Chemistry ...	909 3 5	
2 8 6		Other Publications	1 5 0	
151 19 7		Cheap sets	6 16 0	
	5451 15 4			5437 4 5
663 6 6		,, Proceeds of Advertisements	660 0 11	
197 15 6		*Less* Commission	196 13 4	
	465 11 0			463 7 7
	75 0 0	,, Transfer from General Purposes Account, being Life Composition Fees for year		— — —
	247 10 0	,, Donations		511 15 0
	700 0 0	,, Government Publications Grant (through the Royal Society)		700 0 0
	330 16 11	,, Dividends on Investments		306 19 6
	96 0 11	,, Income Tax recovered		89 6 0
	7 11	,, Interest on Deposit		5 4
	5906 0 4	,, Transfer from General Purposes Account (the balance of expenditure on publications) ...		5841 19 1
	£13,273 2 5			£13,350 16 11

Expenditure.

1935 £ s. d.	1935 £ s. d.	Expenditure.	1936 £ s. d.	1936 £ s. d.
		By Expenses on account of Journal:—		
1159 9 7		Editorial Salaries	1159 18 9	
85 12 6		Superannuation	85 12 6	
35 0 9		Editorial Postages	33 1 0	
3367 13 4		Printing, Paper, etc.	3316 1 8	
562 11 0		Distribution	558 13 5	
352 9 6		Authors' Copies	343 13 6	
18 10 3		Miscellaneous	18 11 8	
	5581 6 11			5515 12 6
		,, Expenses on account of Abstracts:		
1318 3 6		Editorial Salaries	1304 15 4	
20 18 10		Superannuation	20 18 10	
77 5 8		Editorial Postages	79 19 6	
1526 18 2		Abstractors' Fees	1536 16 10	
3453 7 2		Printing, Paper, etc.	3571 4 11	
376 12 3		Distribution	363 6 1	
93 10 9		Miscellaneous	95 12 6	
	6866 16 4			6972 14 0
		,, Annual Reports on the Progress of Chemistry:		
727 10 2		Printing and Honoraria	862 10 5	
22 9 0		Advertising	— — —	
	749 19 2			862 10 5
		,, Carried to Balance Sheet of Publications Fund, viz.:		
	75 0 0	Life Composition Fees		— — —
	£13,273 2 5			£13,350 16 11

LIBRARY.

Income.

1935 £ s. d.	1935 £ s. d.	Income.	1936 £ s. d.	1936 £ s. d.
		To Donations:		
100 0 0		Association of British Chemical Manufacturers	100 0 0	
21 0 0		Biochemical Society	21 0 0	
15 15 0		Faraday Society	15 15 0	
50 0 0		Institute of Brewing	50 0 0	
250 0 0		Institute of Chemistry	646 10 0	
100 0 0		Society of Chemical Industry	448 0 0	
10 10 0		Society of Dyers and Colourists	10 10 0	
21 0 0		Society of Public Analysts	21 0 0	
8 0 0		Fellows	3 0 0	
	576 5 0			1315 15 0
	8 10 11	,, Miscellaneous receipts		7 10 3
	1869 10 4	,, Contribution from General Purposes Account		1203 0 7
	£2454 6 3			£2526 5 10

Expenditure.

1935 £ s. d.	Expenditure.	1936 £ s. d.
1367 8 9	By Salaries and Wages	1403 2 0
162 16 0	,, Superannuation of Library Staff	162 3 0
686 12 5	,, Books and Periodicals *	649 3 6
137 1 6	,, *Binding*	147 18 3
63 3 6	,, Printing, Stationery and Postages (proportion)	54 11 10
92 9 7	,, House Expenses, etc. (proportion)	100 4 9
42 16 5	,, Special Printing, etc. (Nathan Collection)	— — —
11 18 1	,, Miscellaneous	9 7 0
£2454 6 3		£2526 5 10

* Other than those received in exchange.

RESEARCH FUND.

Income

1935 £ s. d.		1936 £ s. d.
490 9 2	To Dividends on Investments	491 4 0
140 2 11	,, *Income Tax recovered*	129 7 10
80 14 8	,, Repayment of Grants	34 2 0
10 0 0	,, Grants not applied for	4 0 0
1 13 2	,, Interest on Deposit	1 7 4
5 10 0	,, Sale of Apparatus	— — —
90 0 0	,, Legacy	— — —
1142 16 0	,, Repayment at par of £1,142 16*s.* 0*d.* New South Wales 3% Stock ...	— — —
17 7 6	,, Balance, being Excess of Expenditure over Income, carried to *Balance* Sheet	— — —
£1978 13 5		£660 1 2

Expenditure

1935 £ s. d.		1936 £ s. d.
— — —	By Honorarium, Longstaff Medallist	20 0 0
— — —	,, *Longstaff Medal*	2 0 0
740 0 0	,, Grants	622 0 0
5 17 5	,, Miscellaneous Expenses	8 8 10
1232 16 0	,, Purchase of £1,146 13*s.* 1*d.* Conversion Stock 3½%	— — —
— — —	,, Balance, being Excess of Income over Expenditure, carried to Balance Sheet	7 12 4
£1978 13 5		£660 1 2

Income and Expenditure Accounts of other Funds for the Year ended 31st December, 1936.

SPECIAL PUBLICATIONS FUND.

Income.

1935 £ s. d.	1935 £ s. d.		1936 £ s. d.	1936 £ s. d.
		To Sales of Publications:		
61 0 0		Abstract "A" printed on one side of the paper	70 0 0	
11 1 6		Memorial Lectures, Vol. I. ...	10 17 6	
7 12 9		Do. Vol. II. ...	10 9 0	
7 16 11		Do. Vol. III. ...	9 10 10	
3 0		List of Fellows ...	4 12 0	
8 3		Portraits ...	1 19 6	
5 4 6		Faraday Lectures ...	5 1 2	
1 8 0		Perkin Memorial Volume ...	1 0 0	
—		Discussion Number ...	1 4	
1 0		Fourth Pedler Lecture ...	—	
8 0		Fifth Liversidge Lecture ...	—	
—	95 1 11	Lecture on "Modern Chemical Nomenclature"	23 17 7	137 8 11
	65 14 2	,, Dividend on Investments ...		74 0 8
	2 0 4	,, Interest on Deposit ...		2 18 0
	16 13 0	,, Income Tax recovered ...		—
	—	,, Excess of Expenditure over Income carried to Balance Sheet ...		52 6 0
	£179 9 5			£266 13 7

Expenditure.

1935 £ s. d.		1936 £ s. d.
64 15 11	By Production of Abstracts "A" printed on one side of the paper ...	67 3 5
—	Do. List of Fellows ...	153 8 1
3 13 0	,, Reprints for Memorial Lectures, Vol. IV. ...	15 1 10
—	,, Do. Faraday Lectures, Vol. II. ...	3 4 9
2 4 3	,, Do. of Fifth Liversidge Lecture ...	—
—	,, Do. Lecture on "Modern Chemical Nomenclature" ...	27 15 6
37 10 0	,, Contribution towards the collected works of the late Sir William Hardy	—
71 6 3	,, Balance, being Excess of Income over Expenditure, carried to Balance Sheet ...	—
£179 9 5		£266 13 7

SPECIAL LECTURES FUND.

Income.

1935 £ s. d.		1936 £ s. d.
37 15 3	To Dividends on Investments ...	40 2 7
10 4 6	,, Income Tax recovered ...	5 4 0
6 0	,, Interest on Deposit ...	14 5
—	,, Balance, being Excess of Expenditure over Income, carried to Balance Sheet ...	21 15 10
£48 5 9		£67 16 10

Expenditure.

1935 £ s. d.		1936 £ s. d.
25 0 0	By Honoraria ...	50 0 0
9 16 0	,, Lecture Expenses ...	16 7 6
10 6	,, Miscellaneous Expenses ...	1 9 4
12 19 3	,, Balance, being Excess of Income over Expenditure, carried to Balance Sheet ...	—
£48 5 9		£67 16 10

STAFF PENSIONS FUND.

Income.

1935 £ s. d.		1936 £ s. d.
74 16 3	To Transfer from General Purposes Account ...	77 12 4
35 13 7	,, Dividends on Investments ...	38 4 0
9 11 2	,, Income Tax recovered ...	4 3 8
£120 0 0		£120 0 0

Expenditure.

1935 £ s. d.		1936 £ s. d.
120 0 0	By Pension paid during 1936 ...	120 0 0
£120 0 0		£120 0 0

THE EDWARD FRANK HARRISON MEMORIAL TRUST FUND.

Income.

1935 £ s. d.		1936 £ s. d.
41 1 3	To Dividends on Investments ...	40 15 0
11 5 11	,, Income Tax recovered ...	11 5 10
1 0 0	,, Interest on Deposit ...	13 0
—	,, Excess of Expenditure over Income carried to Balance Sheet ...	105 12 8
£53 7 2		£158 6 6

Expenditure.

1935 £ s. d.		1936 £ s. d.
3 4 0	By Advertising ...	150 0 0
—	,, Harrison Prize ...	6 15 0
—	,, Harrison Plaque ...	1 11 6
—	,, Miscellaneous Expenses ...	—
50 3 2	,, Balance, being Excess of Income over Expenditure, carried to Balance Sheet ...	—
£53 7 2		£158 6 6

THE CHEMICAL SOCIETY.—BALANCE SHEETS, 31st December, 1936

GENERAL PURPOSES.

1935 £ s. d.	1935 £ s. d.	*Liabilities.*	1936 £ s. d.	1936 £ s. d.
	922 7 6	To Subscriptions received in advance ...		1,044 1 6
	4,372 4 2	,, Sundry Creditors (Printing and other Expenses)		3,246 5 8
22,883 9 5		,, Excess of Assets over Liabilities as per last Balance Sheet	21,241 9 4	
1,642 0 1		*Deduct* Excess of Expenditure over Income for Year	302 19 10	
			20,938 9 6	
— — —		*Add* Transfer from Publication Fund	1,863 0 0	
— — —		,, Life Composition Fees (two-thirds)	269 11 5	
	21,241 9 4			23,071 0 11
	116 17 10	,, Current Account at Bankers (overdrawn)		202 3 6
	— — —	,, Herbert Spencer Bequest, unexpended Balance		931 16 6
	£26,652 18 10			£28,495 8 1

1935 £ s. d.	*Assets.*	1936 £ s. d.
25,854 5 1	By Investments as per Schedule (*cost or value when acquired*)	27,717 5 1
407 8 4	,, Sundry Debtors	431 6 6
350 0 0	,, Subscriptions in Arrear, £467 14*s.* 0*d.* Estimated to realise	320 0 0
41 5 5	,, Cash in hand	26 16 6
£26,652 18 10		£28,495 8 1

PUBLICATIONS FUND.

1935 £ s. d.	1935 £ s. d.	Liabilities		1936 £ s. d.	1936 £ s. d.
11,275 0 11		To Excess of Assets over Liabilities as per last Balance Sheet		11,350 0 11	
75 0 0		*Add* Amount transferred from Income and Expenditure Account for Investment		— — —	
— — —		*Less* Transferred to General Account	1,863 0 0		
— — —		Do. uninvested Composition Fees	123 17 1		
				1,986 17 1	
	11,350 0 11				9,363 3 10
	£11,350 0 11				£9,363 3 10

1935 £ s. d.	Assets	1936 £ s. d.
11,226 3 10	By Investments as per Schedule (cost or value when acquired)	9,363 3 10
123 17 1	,, Cash at Bank	— — —
£11,350 0 11		£9,363 3 10

RESEARCH FUND.

1935 £ s. d.	1935 £ s. d.	*Liabilities.*	1936 £ s. d.	1936 £ s. d.
	760 0 0	To Sundry Creditors		632 0 0
14,483 17 10		,, Excess of Assets over Liabilities as per last Balance Sheet...	14,699 6 4	
142 16 0		*Add* Profit on Redemption of New South Wales 3% Stock	— — —	
90 0 0		,, Legacy	— — —	
14,716 13 10				
— — —		*Add Excess of Income over Expenditure for year*	7 12 4	
				14,706 18 8
17 7 6		*Less Excess of Expenditure over Income for year*		— — —
	14,699 6 4			
	£15,459 6 4			£15,338 18 8

1935 £ s. d.	*Assets.*	1936 £ s. d.
14,675 18 0	By Investments as per Schedule (cost or value when acquired)	14,675 18 0
783 8 4	,, Cash at Bank	663 0 8
£15,459 6 4		£15,338 18 8

THE CHEMICAL SOCIETY. BALANCE SHEETS, 31ST DECEMBER, 1936

SPECIAL PUBLICATIONS FUND.

£ s. d.	£ s. d.		£ s. d.	£ s. d.
	48 0 0	To Amount prepaid for 1937		10 5 0
	25 4 6	" Sundry Creditors		174 14 9
		" Sinking Fund for Collective Index (1923–32)		
311 5 4		as per last Balance Sheet		— — —
488 2 11		*Add* Transfer from General Purposes		— — —
11 9		" Interest		— — —
800 0 0				
800 0 0	— — —	*Less* Paid on Account to Bureau of Chemical Abstracts		— — —
		" Excess of Assets over Liabilities as per last		
1921 5 10		Balance Sheet	1992 12 1	
71 6 3		*Add* Excess of Income over Expenditure for Year	— — —	
— — —	1992 12 1	*Less* Excess of Expenditure over Income for Year	52 6 0	1940 6 1
	£2060 16 7			£2125 5 10

£ s. d.		£ s. d.
1600 0 0	By Investment as per Schedule (cost or value when acquired)	1600 0 0
460 16 7	" Cash at Bank	525 5 10
£2060 16 7		£2125 5 10

SPECIAL LECTURES FUND.

£ s. d.	£ s. d.		£ s. d.	£ s. d.
		To Excess of Assets over Liabilities as per last		
1075 9 4		Balance Sheet	1088 8 7	
12 19 3		*Add* Excess of Income over Expenditure for year	— — —	
— — —	1088 8 7	*Less* Excess of Expenditure over Income for year	21 15 10	1066 12 9
	£1088 8 7			£1066 12 9

£ s. d.		£ s. d.
1000 0 0	By Investment as per Schedule (cost or value when acquired)	1000 0 0
88 8 7	" Cash at Bank	66 12 9
£1088 8 7		£1066 12 9

STAFF PENSIONS FUND.

£ s. d.		£ s. d.
907 14 0	To Excess of Assets over Liabilities as per last Balance Sheet	907 14 0
£907 14 0		£907 14 0

£ s. d.		£ s. d.
902 13 9	By Investments as per Schedule (cost or value when acquired)	902 13 9
5 0 3	" Cash at Bank	5 0 3
£907 14 0		£907 14 0

THE EDWARD FRANK HARRISON MEMORIAL TRUST FUND.

£ s. d.	£ s. d.		£ s. d.	£ s. d.
	1 2 6	To Sundry Creditors		— — —
		" Excess of Assets over Liabilities as per last		
1219 5 10		Balance Sheet	1269 9 0	
50 3 2		*Add* Excess of Income over Expenditure for year	— — —	
— — —	1269 9 0	*Less* Excess of Expenditure over Income for year	105 12 8	1163 16 4
	£1270 11 6			£1163 16 4

£ s. d.		£ s. d.
1101 7 11	By Investments as per Schedule (cost or value when acquired)	1101 7 11
169 3 7	" Cash at Bank	62 8 5
£1270 11 6		£1163 16 4

SCHEDULE OF INVESTMENTS.

GENERAL PURPOSES.

Nominal Details.	*Cost or Value when Acquired.* £ s. d.	*Market Value 31st December, 1936.* £ s. d.
£787 London, Midland and Scottish Railway 4% Debenture Stock	839 3 7	846 0 6
£1520 14s. 3d. Cardiff Corporation 3% Stock, 1914/54	1650 0 0	1520 14 3
£1400 India 2½% Stock	1316 1 0	1008 0 0
£2400 Bristol Corporation 3½% Debenture Stock, Bristol Dock Account	2070 2 0	2232 0 0
£2718 London, Midland and Scottish Railway 4% Preference Stock	3572 0 4	2482 7 11
£1200 Leeds Corporation 3% Stock	1143 1 0	1158 0 0
£1096 6s. 2d. Union of South Africa 3% Stock, 1954/64	1067 12 10	1107 5 5
£1200 London and North Eastern Railway 3% Debenture Stock ...	1033 11 0	1002 0 0
£700 Canada 3½% Stock, 1930/50	704 8 6	707 0 0
£2529 6s. 9d. 5% Conversion Loan, 1944/64	2446 2 6	2968 16 2
£1100 5% ditto ditto ditto	1045 0 2	1291 3 6
£600 4% Funding Loan, 1960/90	480 0 0	697 10 0
£12,926 9s. 0d. 3½% Conversion Stock 1961, or after	10,350 2 2	13,750 10 3
	£27,717 5 1	£30,771 7 0

PUBLICATIONS FUND.

£5260 19s. 9d. 3½% Conversion Stock, 1961, or after	3645 13 8	5596 7 6
£3173 1s. 6d. 5% Conversion Loan, 1944/64	3199 18 7	3724 7 11
£817 P. & O. Steam Navigation Co. Deferred Stock	2060 0 0	1225 10 0
£603 London, Midland and Scottish Railway 4% Guaranteed Stock	457 12 7	630 2 9
	£9,363 3 10	£11,176 8 2

RESEARCH FUND.

Nominal Details.	*Value or Cost when Acquired.* £ s. d.	*Market Value 31st December, 1936* £ s. d.
£1000 London and North Eastern Railway 4% 2nd Guaranteed Stock	1010 0 0	975 0 0
£1034 Great Western Railway 2½% Debentures	1049 15 11	780 13 5
£1122 Metropolitan Water Board 3% "B" Stock	1002 16 9	1110 15 7
£1483 London, Midland and Scottish Railway 4% Debenture Stock	1508 3 6	1594 4 6
£806 Victoria 3% Stock, 1929/49	706 6 2	797 18 10
£4498 11s. 0d. 5% Conversion Loan, 1944/64	4267 4 10	5280 3 6
£6311 6s. 10d. 3½% Conversion Stock, 1961, or after	5131 10 10	6713 13 9
	£14,675 18 0	17,262 9 7

SPECIAL PUBLICATIONS FUND.

£2115 8s. 10d. 3½% Conversion Stock, 1961, or after	£1600 0 0	£2250 6 0

SPECIAL LECTURES FUND.

£1299 9s. 4d. 3½% Conversion Stock, 1961, or after	£1000 0 0	£1382 6 1

STAFF PENSIONS FUND.

£683 6s. 1d. 3½% Conversion Stock, 1961, or after	527 13 9	726 17 3
£371 17s. 1d. 5% Conversion Loan, 1944/64	375 0 0	436 9 3
	£902 13 9	£1163 6 6

THE EDWARD FRANK HARRISON MEMORIAL TRUST FUND.

£61 15s. 8d. 3½% Conversion Stock, 1961, or after	50 1 5	65 14 5
£1255 London, Midland and Scottish Railway 4% Debenture Stock	1051 6 6	1349 2 6
	£1101 7 11	£1414 16 11

I have examined the above Balance Sheets and accompanying Income and Expenditure Accounts with the Books and Vouchers of the Society, and certify them to be in accordance therewith. I have also verified the Balances at the Bankers and the Investments. The figures relating to the Bureau of Chemical Abstracts are included in the above accounts subject to the production of certified accounts by the Bureau.

23, Queen Victoria Street, E.C. 4.
17th February, 1937.

W. B. Keen.
Chartered Accountant.

Approved { George Senter, H. D. K. Drew, H. B. Cox

PRESIDENTIAL ADDRESS.

Delivered at the Annual General Meeting, March 18th, 1937.

By N. V. Sidgwick, C.B.E., M.A., D.Sc., F.R.S.

Hybrid Molecules.

In my remarks at the annual meeting at Bristol last year, I said something about the modifications which structural chemistry has undergone in the last few years through the introduction of the concept of resonance. These modifications are so important to all sides of chemistry that I think I cannot do better this year than say something more about them.

I may briefly repeat what is meant by resonance in organic chemistry. If a molecule can be represented by two (or more) structural formulæ (in the ordinary sense of that term), and if these formulæ ascribe approximately the same positions to the atoms and are of about the same stability or energy content, then it is found that the actual state of the molecule is not that represented by either of the formulæ, but is something between them, which cannot be expressed by means of the ordinary structural symbols; it has to some extent the properties of both, but is more stable than either, and also the linked atoms are rather nearer together than is usual. If the structures differ in stability, the actual state will lie nearer to the more stable. This phenomenon is known as resonance, and the molecule is then said to be a resonance hybrid of the two (or more) forms.

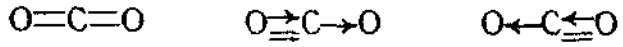
The idea that a molecule may have a structure intermediate between those represented by two ordinary formulæ is certainly not new: Kekulé's conception of the benzene nucleus, and Conrad Laar's idea of tautomerism in general involve something like this, and a more definite approach to it is the "valency tautomerism" of Wieland and others (Wieland, *Ber.*, 1920, **53**, 1318; see also Arndt and Eistert, *Z. physikal. Chem.*, 1935, *B*, **31**, 125).

But the theory of resonance differs from these general notions in two specific particulars. It demands that the two formulæ should have their atoms in very nearly the same positions, and makes resonance impossible if the change from one to the other involves any serious shift even of a hydrogen atom. Further it shows that when resonance occurs the resulting molecule is more—often much more—stable than either of the component structures. Now this conclusion is one which could not have been anticipated from general considerations, or calculated by classical mechanics. It is impossible to understand why these things are so unless one has some knowledge of the principles of wave mechanics, and it is impossible to discover the quantitative results of the theory unless one is familiar with the methods of wave-mechanical calculations.

This at once raises a difficulty. The general conclusions of the theory of resonance are of great practical importance, especially to the organic chemist. But it is not to be expected that more than a very few organic chemists will have either the time or the ability to master these mathematical operations. It is therefore obviously our duty to express—or to induce the wave-mechanicians to express—the results in the simplest terms that are possible, and this can really be done quite easily. The use of the technical language of wave mechanics for this purpose is quite unnecessary and in fact misleading, for it makes the non-mathematical reader think that as he can't understand the language he can't understand the conclusions either, which is quite untrue; and not uncommonly, I think, it leads the non-mathematical writer to believe that if he knows the technical terms he must understand their meaning, which is by no means always the case. It was well said by Clerk Maxwell:* "For the sake of persons of different types of mind scientific truth should be presented in different forms, and should be regarded as equally scientific whether it appears in the robust form and colouring of a physical illustration, or in the tenuity and paleness of a symbolical expression."

* Quoted by Sir J. J. Thomson, "Recollections," p. 392.

For example, with carbon dioxide we have the three formulæ



According to the theory of resonance, since all these formulæ represent linear molecules, and should have about the same stability or heat of formation, resonance must occur, and the actual state of the molecule will be something intermediate between them which we call a resonance hybrid, which will have a greater stability and heat of formation, and a rather smaller distance between the atoms, than correspond to any one of the formulæ. Experiment shows that this is so. Further, since the last two formulæ are really the same, they must be represented to the same extent in the actual state of the hybrid, which therefore should be non-polar, as it is found to be.

These ideas are simple enough, and they gain nothing in clearness for the ordinary chemist if they are expressed in the technical language of wave mechanics—if I say that in the carbon dioxide molecule we have a superposition of eigenfunctions, that the three formulæ I have given are the unperturbed canonical structures, and that the last two are completely degenerate : it is better to say that these are the three constituent formulæ, that the last two are the same, and that carbon dioxide is a resonance hybrid between the three.

Another terminological difficulty arises from the word resonance itself. This undoubtedly suggests to the ordinary man a rapid alternation between two structures, an idea that presents itself the more readily since we are already familiar with it in tautomerism. But this is not what resonance means : it must be sharply distinguished from rapid tautomerism. In tautomerism, the substance is a mixture of two kinds of molecules in equilibrium after the manner of a reversible chemical reaction ; the rate of change may be too quick to be measured, but it is quite definite, and further there is no reason why some of the atoms, especially of the hydrogen atoms, should not change their positions in going from one tautomeric form to the other. Also the occurrence of tautomerism is not necessarily a sign of greater stability, but rather the opposite. In resonance on the other hand there is no chemical change, quick or slow : the substance is not a mixture, but all the molecules are in a state intermediate between those represented by the constituent formulæ : the positions of the atoms in these formulæ must be nearly the same, and the occurrence of resonance necessitates an increase in the stability of the molecule.

It would therefore I think be better if we could adopt another name, and mesomerism, which has been applied to the phenomenon by Prof. Ingold, seems to be the most suitable. It is however of little use for the chemist to adopt this unless the physicists who are specially concerned with the problem will do the same.

Some of the more important applications of the idea of resonance I considered last year, especially its close relation to the modern theories of organic reactivity. Another point is the so-called co-ordination of hydrogen, which accounts for the association of hydroxyl compounds. There is no doubt that a hydrogen atom is able to hold two oxygen atoms together, and the crystallographers have actually measured the length of this O—H··O link (about 2·5 A.), which they call the hydrogen link,* but the idea which formerly prevailed, that this link, like co-ordinate links in general, was due to the hydrogen taking up two more shared electrons (so that it had four in all), is now known to be impossible, since a hydrogen atom cannot hold four electrons with sufficient firmness. The only alternative explanation is that we have resonance between the ordinary form and one in which there is an oxonium cation and an R–O anion :

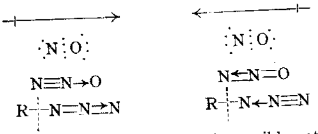
I will not discuss this, except to point out that the condition of the resonance, and hence of the gain of energy which accompanies it, is that the atoms should retain their positions ;

*** For further details, see Bernal and Megaw, *Proc. Roy. Soc.*, 1935, 151, 384.**

hence the ions in the ionised structure are not free to move, and so cannot contribute to the electrical conductivity of the liquid.

One advantage which we have in these days is that any theory of structure can be tested by the measurement of a whole series of properties. This is eminently true of resonance. When the attempt was first made, some eight or ten years ago, to determine the magnitude of the various properties of covalent links, it was evident that this could only be successful if these properties were at least approximately constant—if they were more or less independent of the other links in the molecule. It is now clear that to a large extent this is so, but that the properties are considerably modified when there is resonance in the molecule. Conversely the departure of these properties of links from their normal values provides the best evidence we have of the occurrence of resonance. The properties which are most frequently used for its detection are, as we have seen, the heats of formation and the internuclear distances; but in addition we can use the dipole moments, the force constants of the links, and the general reactivity. These points are best illustrated by taking a series of examples.

It happens with several molecules that there is a possibility of two structural formulæ, conforming to the conditions of resonance, both of which have large dipoles, but in opposite directions, and that the actual molecule can be shown to have a very small moment: as for example with nitric oxide, nitrous oxide, and the organic azides:



Dipole moment.

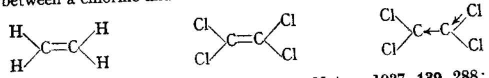
0·16 D

0·17 D

N_3 *ca.* 0

The very small moment observed is impossible not only for each structure separately, but also for any mixture of the two in tautomeric equilibrium in the ordinary sense: a mixture of two highly polar substances, even if their moments are in opposite directions, will itself be highly polar, as it does not matter to the dielectric constant which way the dipole is pointing; but if the molecule is in a state intermediate between the two structures, their opposing dipoles will tend to neutralise one another.

With some molecules we can make use of the force constants of the links. These constants, which are derived from the absorption spectra, are a measure of the resistance of the link to deformation, and may be said to throw more light on the actual state of the molecule than the heats of formation, since they can be determined for individual links and not merely for the molecule as a whole. A comparison of the values of these properties for ethylene and for tetrachloroethylene is very instructive. In ethylene itself no resonance is possible: every hydrogen atom already carries its maximum load of electrons, and they are all shared. But in tetrachloroethylene there is a possibility of the formation (as in chlorobenzene) of a double link between a chlorine and a carbon, as shown below:



The values of the force constants are (see Duchesne, *Nature*, 1937, **139**, 288; Linnett and Thompson, *ibid.*, p. **509**):

C—H in methane $4{\cdot}98 \times 10^5$	C=C in ethylene $9{\cdot}0 \times 10^5$	C—Cl in CCl_4 $3{\cdot}8 \times 10^5$
C—H in ethylene 4·85 ,,	C=C in C_2Cl_4 5·8 ,,	C—Cl in C_2Cl_4 5·2 ,,

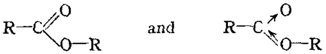
There could not be clearer evidence that while the C—H link is the same in ethylene as it is in methane, the C—Cl link is stronger in tetrachloroethylene than it is in carbon tetrachloride, and becomes so at the expense of the double carbon link. The measurements of the length of the C=C link appear to be in agreement with this; in ethylene it has been

found (Scheib and Lueg, *Z. Physik*, 1933, **81**, 764) to be 1·34 A., and in tetrachloroethylene 1·38 A. (Brockway, *Rev. Mod. Physics*, 1936, **8**, 261).

Of the large number of organic structures whose behaviour is determined by resonance we may consider two, the carbonyl group >C=O, and the most important of all, the aromatic ring. The most familiar examples of carbonyl compounds are : (1) aldehydes and ketones, (2) carboxylic acids and their derivatives, such as the esters and amides, (3) carbon dioxide (carbon monoxide might be included, but its resonance does not concern us at the moment). Organic chemists have long been aware that the carbonyl group in an ester is very different in behaviour from that in an aldehyde or ketone, and much less active. It does not give the carbonyl reactions with hydroxylamine or phenylhydrazine, it is much less easily reduced, and its refractive power and its parachor are less than we should expect. Again, two adjacent carbonyls in the α-diketones give the compound an intense yellow colour, as we see in diacetyl, glyoxal, and benzil; but pyruvic acid and oxalic acid are colourless. Carbon dioxide behaves in general like the acids and esters rather than the aldehydes and ketones.

It was at one time supposed that these peculiarities of the acids were due to the hydrogen of the carboxyl group being in some way joined to both oxygens; but nearly all these properties are shared by the esters, where no such explanation is possible. There should obviously be some explanation applicable to the acids and their esters and to carbon dioxide, but not to aldehydes and ketones. This is given quite simply by the theory of resonance. We have already seen how this is possible in carbon dioxide, and its occurrence is proved both by the heat of formation, which is 30 kg.-cals. higher than one would calculate, and by the O . . . O distance, which is found to be only 2·30 A., whereas one would calculate it on any of the three formulæ to be 2·56 A.

With the acids and their derivatives there is a similar possibility of resonance between the structures

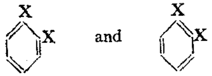


This is supported by their heats of formation; Pauling and Sherman (*J. Chem. Physics*, 1933, **1**, 606) have shown that the resonance energy, that is, the excess of the observed over the calculated heat of formation, is on the average about 27 kg.-cals. for the carboxylic acids and about 23 kg.-cals. for their esters, and rather less for their amides (the heat of formation of a single link is usually between 50 and 100 kg.-cals.).

One important point must be mentioned here. The result of the resonance is, as we have seen, an increase in the heat of formation and therefore in the stability of the molecule. Hence the resonance hybrid will in general be less reactive than the usual formula would imply, even when the second formula looks as if it would be more reactive; this appears very clearly in these acid derivatives, where the CO group is much less active when resonance is possible than it is in the ketones where it is not.

At the same time we must recognise that the resonance, while it increases the stability and heat of formation of the molecule as a whole, may diminish that of a particular link, as we have seen in tetrachloroethylene.

The most extensive group of organic substances whose behaviour is determined by resonance is that of the aromatic compounds. It was recognised from the beginning that the two difficulties in the way of Kekulé's formula for benzene are, first, that we should expect two ortho-di-derivatives



and secondly, that benzene should have the reactivity of an ethylene derivative, whereas in fact it behaves almost always as a saturated compound. The conception of resonance removes both of these objections at once : the first because we assume the state of the ortho-compound to be permanently half way between the two formulæ, and the second

on account of the increased stability which the resonance must produce. The last point can be determined experimentally from the heats of formation, and the following table gives the values of the resonance energy, as found by Pauling and Sherman (*loc. cit.*), first the value for the whole molecule, and secondly the amount per aromatic ring : it will be seen that the values of this last figure are approximately constant.

Resonance Energy of Aromatic Compounds.

Compound.	Resonance energy, in kg.-cals.	Resonance energy / Number of rings, in kg.-cals.	Compound.	Resonance energy, in kg.-cals.	Resonance energy / Number of rings, in kg.-cals.
Benzene	37·6	37·6	Acenaphthene ...	70·8	35·4
Toluene	39·2	39·2	Anthracene	104·7	34·9
Ethylbenzene ...	39·7	39·7	Phenanthrene ...	110·2	36·7
Propylbenzene ...	41·3	41·3	Chrysene	150·6	37·7
Naphthalene	74·7	37·4			

These results are based on the heats of combustion. The theoretical calculation (Pauling and Wheland, *J. Chem. Physics.*, 1933, **1**, 362) shows that in benzene three other structures, more or less corresponding to the Dewar formulæ, have to be taken into account, but that over 80% of the resonance energy is due to the two Kekulé structures. In the same way in naphthalene, where there are altogether 42 structures to be taken into account, 68% of the resonance energy is due to the three obvious formulæ

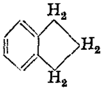
This conception of the aromatic ring explains many of its peculiarities, and especially its extreme adaptability. This is indeed proved directly by the high refractive power, but it is shown in many other ways as well. Thus the electrons attaching atoms to the ring can be moved towards or away from it; it has been shown (Sutton, *Proc. Roy. Soc.*, 1931, **133**, 668) that the electron drift, as indicated by the difference in electrical dipole moments between an aromatic compound and its aliphatic analogue, is what determines the position of further substitution, a conclusion which the organic chemists had already reached on grounds of reactivity alone.

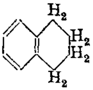
An interesting question is how far the resonance in benzene is affected by the presence of other groups in the molecule. Normally a substituent if it produces any effect will cause an increase, by providing new resonance structures. Pauling and Sherman (*loc. cit.*) have given a series of values (derived from the heats of formation) of the extra energies of the compounds $C_6H_5 - X$: some of these are quoted below.

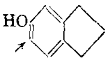
X.	Extra energy.	X.	Extra energy.	X.	Extra energy.
$-CH_3$	1·6	$-O-CH_3$	6·0	$-NH_2$	4·4
$-C_2H_5$	1·9	$-CHO$	3·5	$-NHCH_3$	6·2
$-CH{=}CH_2$	6·7	$-CO-CH_3$	7·2	$-CN$	4·8
$-C{\equiv}CH$	10·4				

On the other hand it would appear that it is sometimes possible to reduce the resonance by steric effects. This was first suggested by Mills and Nixon (J., 1930, 2510) before the resonance theory had been developed. They pointed out that on stereochemical grounds we might expect that in hydrindene (I) (with a reduced 5-ring attached to the nucleus) the most stable form would be that which had a single link common to the two rings, while in tetralin (II) (with a 6-ring) the common link should be double. They obtained experimental confirmation of this by showing that if 5-hydroxyhydrindene (III) is brominated or coupled with diazo-compounds, reaction takes place at carbon atom 6, whereas in the corresponding tetralin derivative (IV) it occurs in the α-position. Both these reagents would be expected to attack the carbon atom joined to the hydroxylic carbon atom by a double link. This work has been carried further by Fieser and Lothrop (*J. Amer. Chem. Soc.*, **1936**, **58**, 2050), who tried the effect on the coupling with diazo-compounds of blocking the natural positions with methyl groups. They found that with the hydrindene compound (V) *no*

coupling occurred at all, whereas the tetralin derivative (VI) coupled readily in the position shown by the arrow.


(I.)


(II.)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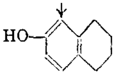
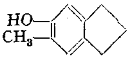
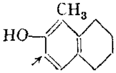
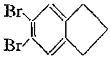
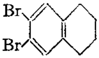

(IV.)

(V.)



(VI.)

These results suggest that Mills and Nixon's conclusions are valid for hydrindene but not for tetralin; this is what we might expect, since the strain in tetralin can be relieved if the reduced ring is not planar, whereas no such relief is possible in hydrindene. Further confirmation is afforded by the dipole moments of the dibromo-derivatives of the two systems (VII and VIII).


(VII.)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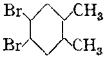
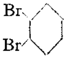

(IX.)


(X.)

It is evident that if the double links are fixed in the positions suggested (as shown in the diagram) the angle between the C—Br valencies will be greater (and hence the moment smaller) in the hydrindene compound, and least in the tetralin, while in the benzene and *o*-xylene derivatives (IX and X), where resonance must prevail, it should have an intermediate value. Experiment showed (Sidgwick and Springall, J., 1936, 1532) that the moment of the $\begin{matrix}\text{Br—C}\\ \text{Br—C}\end{matrix}$ system was practically the same in the benzene, xylene, and tetralin derivatives (X), (IX), and (VIII) (2·12, 2·13, 2·11 D, respectively), but markedly lower (1·78 D) in the hydrindene compound (VII), thus entirely confirming the results of Fieser and Lothrop.

It is to be noticed that the evidence of Fieser and Lothrop, like that of Mills and Nixon, is based on the reactivity, and so depends on the heat of activation, a relatively small change in which may account for the whole effect. Sutton and Pauling (*Trans. Faraday Soc.*, 1935, **31**, 939) have discussed this question from the theoretical side, and conclude that a difference of 6% in the ratio of the coefficients (*i.e.*, in the predominance) of the two Kekulé forms is enough to account for the experimental results of Mills and Nixon. On the other hand the dipole moments express the mean positions of the atoms in the resting molecules, and they certainly show the difference to be expected if the links were fixed in hydrindene but not in tetralin.

It is too early to say definitely whether this conclusion is to be accepted; but if it is, it leads to a remarkable result. The peculiarities of the aromatic compounds—the "aromatic character"—are due partly to the alternation of single and double links, and partly to the resonance. If these conclusions are correct, then in hydrindene the resonance is stopped, while the alternation of links of course remains. The properties of hydrindene and its derivatives should therefore be those which depend on the alternation, and those which are due to the resonance should be absent.

OBITUARY NOTICES.

JOHN KENNETH HAROLD INGLIS.

1877—1935.

By the death in 1935 of John Kenneth Harold Inglis the University of New Zealand lost a gifted and inspiring teacher of chemistry and an able administrator. He was born in Christchurch, New Zealand, in 1877, and was educated in that city, receiving most of his school training at Christ's College and his University training at Canterbury College, which is part of the University of New Zealand. He was granted the B.Sc. degree with honours in chemistry in 1898 and the M.A. degree in 1899. The ensuing two years he devoted to post-graduate and research work in the University of Edinburgh, and was subsequently granted the D.Sc. degree by that University. His research work in Edinburgh was done in collaboration with the late Professor Hugh Marshall, and is described in a joint paper in the *Proceedings of the Royal Society of Edinburgh* for 1902 on "The Action of Silver Salts on Solutions of Ammonium Persulphate." In this, the first published paper with which Inglis was connected, the authors show that through catalytic action by the silver ion the persulphate ion oxidises part of the ammonium ion present to nitrate ion, and that, if the concentration of the silver ion is relatively small, the reduction of the persulphate ion follows the unimolecular law. Inglis then went to the Physikalisch-chemisches Institut of the University of Leipzig, and worked for some time there, chiefly in collaboration with Professor Robert Luther. In 1903, however, he enrolled as a research student in the Chemical Laboratory of University College, London; and in 1904 he was appointed Assistant in Chemistry there under Sir William Ramsay, to fill a vacancy resulting from the appointment of Dr. M. W. Travers to the Chair of Chemistry in the University of Bristol. In 1906 Inglis was appointed Professor of Chemistry in University College, Reading (now the University of Reading); he resigned that position at the end of 1911 on his appointment to the Chair of Chemistry in the University of Otago in Dunedin, one of the constituent colleges of the University of New Zealand. In 1911 he was also admitted by examination to the Fellowship of the Institute of Chemistry of Great Britain and Ireland. He held the Chair of Chemistry at Otago for nearly twenty-four years, until his sudden death by heart failure at the end of 1935 in his fifty-eighth year. In 1915 he married Ethel Joanna, daughter of William Barron of Dunedin; she pre-deceased him in 1929, leaving one daughter, who survives him. Two other children of the marriage died in infancy.

At Leipzig Inglis' work was chiefly on the oxidation potential of ozone and on the electrochemistry of permanganic acid. In the course of this he confirmed the importance of the catalytic action of manganous ion in permanganate reactions. At University College, London, he carried out further work on ozone, including its estimation, apparent solubility in water, and interaction with aqueous hydrogen peroxide. In 1903 he published jointly with W. W. Taylor a paper on the aluminium electrode, in which evidence was adduced that the peculiar anodic behaviour of aluminium is probably due to the impermeability to aluminium ion and sulphate ion of a film of aluminium hydroxide, whereas halogen and several other ions readily pass through such a film.

Inglis' chief work at University College, London, however was on the fractional distillation at low temperatures of liquefied gases and on the application of this method, previously used by Ramsay and Travers in their classical work on the inert gases, to the analysis of complex gaseous mixtures. The most important outcome of this work was its application by Inglis to a detailed study of the sources of loss of combined nitrogen in the chamber process for making sulphuric acid, with the assistance of Messrs. Spencer, Chapman and Messel, Ltd. By careful analyses of the chimney gases from the chamber plant he showed that the loss is due chiefly to incomplete absorption of nitrogen peroxide and nitric oxide in the Gay Lussac tower, and that reduction to nitrous oxide causes less than one-tenth of the total loss. The analytical difficulties arose from the fact that the chimney gases contained besides nitrogen and oxygen small and variable amounts of carbon dioxide,

nitrous and nitric oxides, nitrogen trioxide, nitrogen peroxide, sulphur di- and tri-oxides, and the vapour of sulphuric acid. During the same period Inglis, jointly with J. E. Coates, made careful measurements of the density of liquid nitrogen and liquid oxygen and of mixtures of these, from which it appeared that, whereas liquid nitrogen was normal, liquid oxygen was about one-tenth polymerised.

At Reading Inglis and his pupils carried out work on the conductivities of α-oximino-fatty acids, the electrolytic chlorination of aromatic organic acids, and the optical properties of compounds containing asymmetric carbon atoms with all four valencies directly attached to carbon. In the last compounds it was expected that racemisation of optically active members would be less pronounced than in compounds in which one valency of the asymmetric carbon atom is attached to hydrogen; but owing to difficulties in the way of purification only preliminary work was done before Inglis left for New Zealand.

In the University of Otago Inglis was faced with the disability which is unfortunately common in the smaller universities of the Dominions, namely, that the head of a scientific department has to deal with a large and varied amount of teaching and administrative work with such inadequate assistance and facilities that the conditions for research work are most discouraging. Consequently Inglis' activities there were mainly in teaching and administration. He was Chairman of the Professorial Board from 1916—1919; and he took an active share in building up the Faculty of Home Science, which was founded in 1911, the year in which he was appointed to the Chair of Chemistry. His outstanding characteristic was sterling honesty and integrity, and, although at times his directness and singleness of purpose prevented him from quite appreciating the other man's point of view, no one ever failed to respect him. It is safe to say that without exception his former students will mourn his loss. N. T. M. Wilsmore.

THOMAS MARTIN LOWRY.

1874—1936.

Thomas Martin Lowry, who died at Cambridge on November 2nd, 1936, came of an old Cornish family which had been long connected with the Methodist Church; he was born at Low Moor, Bradford, Yorks, on October 26th, 1874, the second son of the Rev. E. P. Lowry, senior Wesleyan Chaplain and staff officer at Aldershot. He was educated at Kingswood School, Bath, and thence passed to the Central Technical College, South Kensington, with a Clothworkers' scholarship in 1893; he was awarded the Fellowship of the City and Guilds of London Institute in 1920. From 1896 to 1913 he was assistant to Prof. H. E. Armstrong and, from 1904 to 1913, Lecturer in Chemistry at the Westminster Training College; he became head of the chemical department in Guy's Hospital Medical School in 1913 and was the first teacher of chemistry in a Medical School to be made a Professor of the University of London. In 1920 he was appointed to the Chair of Physical Chemistry which had just been created in Cambridge with the aid of a benefaction from the Oil Companies, and held this position at his death. He married a daughter of the Rev. C. Wood in 1904 and is survived by his widow, two sons and a daughter.

During his long service with Prof. Armstrong, Lowry gained recognition for his delicate work in organic chemistry. The proficiency which he then acquired as a crystallographer expressed itself later in the aptitude which he displayed in applying exact physical methods of measurement to the solution of chemical problems; he developed a rare instinct for grasping the essentials of any subject which he attacked and for ensuring that the quantitative methods used were devoted to the measurement of something which was clearly defined. The vast mass of quantitative physical data collected by Lowry is thus not of merely ephemeral interest but will provide useful working material for future generations of physical chemists.

Lowry laid the foundations of his lifelong study of optical rotatory power quite early in his career as an investigator by discovering the mutarotation—a term which he introduced—of nitro-*d*-camphor and the stereoisomerism of a number of halogen derivatives

of camphor. He isolated two isomeric π-bromonitro-*d*-camphors which change one into the other in solution until equilibrium is reached, thus furnishing a case of what he termed dynamic isomerism; the interconversion was followed by measurements of the rotatory power. The new technique thus initiated was applied to many cases of dynamic isomerism and the conditions determining the isomeric change were worked out. It was found that under favourable external conditions the mutarotation of nitro-*d*-camphor in chloroform solution can be arrested for some days and that the isomeric change of nitro-*d*-camphor is greatly accelerated in benzene solution by the addition of one part in a million of piperidine. The arrest of the change in chloroform solution is due to oxidation of the solvent and to the formation of products which neutralise the basic catalysts present in minute proportion. It may be noted that nitro-*d*-camphor provided one of the first examples of the catalytic action of bases which cannot be ascribed to the presence of hydroxylic ions and is therefore not covered by the conventional theory developed by Ostwald. The further study of this question led Lowry and Faulkner in 1925 to the discovery that the mutarotation of tetramethylglucose could be arrested in both cresol and pyridine solutions but proceeded almost too rapidly for measurement in a mixture of these two solvents. It was thus shown that the isomeric change is conditioned by the presence of an amphoteric solvent which alone is capable of acting as a complete catalyst of the process.

The migration of a hydrogen ion in such compounds as nitro-*d*-camphor and sugar derivatives depends on the addition and removal of a proton at two opposite poles of the molecule. The type of isomeric change involved in this process was termed *prototropy* by Lowry in 1923, although he regarded it as a special case of *ionotropy*, in which a whole radical migrates from one to another part of a molecule as an anion or a cation. This led him to an extended definition of acids and bases, also advanced independently by Brönsted, in which acid and base are defined respectively as the *proton-donor* and *proton-acceptor*. Lowry also saw that similar conditions prevail in conjugated systems in which opposite charges at the two ends may be neutralised by a migration of an electron throughout the system. The earlier portions of the work on this subject were summarised in a report to the British Association in 1904 and subsequent reports of a Committee of Section B on Dynamic Isomerism from 1905 to 1916; the details are given in a series of some thirty papers published mostly in the *Journal* of the Chemical Society. The results of this work were applied later by Lowry in a number of investigations, as, for instance, in a very complete study of the rotatory powers, densities, electrical conductivities, etc., of nicotine and its derivatives in the pure state and in aqueous solutions.

At the time when the earlier work on mutarotation was in progress little was known about the variation of optical rotatory power with wave-length—in fact hardly anything had been learnt since the death of Biot in 1862. It is perhaps Lowry's greatest contribution to chemical and physical science that he realised that little progress in this field could be made until values of rotatory power were determined over the widest possible range of wave-lengths, instead of for a single arbitrarily-selected point on a dispersion curve. So much had this subject been neglected, that when Drude wished to test his mathematical theory of rotatory power in 1907, the only data available were those for quartz. In 1913, Lowry and Dickson were able to show that the optical rotations of ten simple alcohols could be expressed by *one term* of Drude's equation, namely, $\alpha = k/(\lambda^2 - \lambda_0^2)$. A year later, Lowry showed that *two terms of opposite sign* completely represent the anomalous rotatory dispersion of ethyl *d*-tartrate, thus confirming the conclusion which had been reached many years before by Biot and by Arndtsen that anomalous rotatory dispersion originates in the superposition of two partial rotations of opposite sign and of unequal dispersions. These partial rotations may be due to diverse causes, so that some controversy has resulted as to their origin, but the essential validity of the conception, as represented by Drude's equation, was established beyond doubt. The anomalous rotatory dispersion of tartaric acid and the tartrates formed the subject of the Bakerian Lecture delivered by Lowry and Austin in 1921.

Drude's equation is only applicable to transparent media, for which the limits of its validity coincide with the conditions under which maximum experimental accuracy can be obtained. Lowry reached these limits in the case of quartz, where his measurements

with a column nearly half a metre in length, giving a rotation of nearly 13,000° for the Hg 5461 line, extended down to 2263 A., where the rotation is over 100,000° in one direction, and to 32,000 A. in the other, the latter wave-length lying beyond the first infra-red absorption band. Over this entire range, the rotation of quartz, for about 1,000 wave-lengths, could be expressed with the greatest precision by a Drude equation with two terms of opposite signs together with a small constant. The characteristic frequencies of these two terms lie far in the Schumann region at 1130 and 310 A. respectively, and only a few months before his death Lowry was still exploring the possibility of showing their real existence by direct physical methods.

The validity of Drude's equation having been established, Lowry could proceed to rigid definitions so far as the region of transparency is concerned for normal and anomalous rotatory dispersions, namely where the rotation α, and $d\alpha/d\lambda$ and $d^2\alpha/d\lambda^2$ are of constant sign throughout or where α, $d\alpha/d\lambda$ and $d^2\alpha/d\lambda^2$ all pass respectively through zero values. An alternative classification is to describe as *simple* those dispersions which can be represented by one term, and as *complex* those requiring more than one. In general, however, simple dispersions are usually observed only when the characteristic frequencies of all the partial rotations lie close together in the Schumann region, as, for instance, in the sugar series, where the different asymmetric carbon atoms sometimes, but not always, produce a simple rotation. The effect of additional partial rotations of lower frequency, if present, will then always predominate, and between 1933 and 1935 Lowry found that for the two aldehydic sugars, tetra-acetyl μ-arabinose and penta-acetyl μ-fructose, prepared by Wolfrom, the rotations associated with the carbon atoms completely cancel one another, leaving only the pure simple rotation due to the aldehydic groups.

Another subject which interested Lowry was the conception of induced dissymmetry which he and Walker introduced in 1924. They observed with camphor and other substances, that one of the frequencies appearing in the Drude equation corresponds to the characteristic ultra-violet absorption of the carbonyl group, and hence concluded that the electronic structure of the carbonyl group also becomes dissymmetric under the influence of the asymmetric carbon atom. This introduction of a second (induced) centre of dissymmetry Lowry considered to give rise to anomalous rotatory dispersion in some cases.

In recent years, Lowry extended his work on rotatory dispersion from transparent to absorbing media, *i.e.*, to a study of the Cotton effect, with considerable success. In collaboration with H. Hudson he was able to develop equations which adequately express the course of the dispersion curve throughout the wave-length range covered by an absorption band. These equations were derived from results obtained by W. Kuhn in 1930.

During the War Lowry was largely concerned with the production and use of amatol mixtures and the difficulties which arose in shell-filling owing to the polymorphism of ammonium nitrate. He determined the four transition temperatures between the five solid forms of this salt and ascertained the form of the velocity curve for change of state; he also plotted the equilibrium diagram between ammonium nitrate and water. Another outcome of war-time activities is found in Lowry's studies of the chlorides of sulphur, a subject which had been investigated in Cambridge before his arrival. By a series of freezing-point determinations he was able to prove the existence of the red sulphur dichloride, SCl_2, in solution and to obtain it as a crystalline solid at low temperatures; he found that the proportion of sulphur dichloride present in a sulphur–chlorine system can be measured by its absorption of light of wave-lengths 5200 and 5400 A., to which sulphur monochloride and chlorine are transparent. He also obtained trisulphur tetrachloride, S_3Cl_4, and sulphur tetrachloride, SCl_4, the latter being an almost colourless crystalline solid which dissociates so rapidly that no evidence could be obtained of its existence in the liquid phase. Lowry found that sulphur tetrachloride is anomalous in having a higher dielectric constant in the solid state than when fused, behaviour which points to a change of molecular structure on fusion; this is in harmony with the observation that sulphur tetrachloride cannot be detected in the liquid phase and was interpreted by the equation

$$\underset{\text{Solid}}{[\overset{+}{S}Cl_3]\overset{-}{Cl}} \rightleftharpoons \underset{\text{Liquid}}{SCl_2 + Cl_2}$$

Lowry noted that phosphorus pentachloride similarly has a higher dielectric constant in the solid than in the liquid state; this he also attributed to a difference in molecular structure, which cannot, however, be analogous to the case of sulphur tetrachloride because vapour density determinations show phosphorus pentachloride to exist as such in the gaseous phase. The investigation of the sulphur–chlorine system is complicated by the occurrence of a number of dissociation reactions which proceed at different velocities and are influenced by the presence of catalysts, but Lowry was able to confirm his conclusions by measurements of the dielectric constants, densities, surface tensions and parachors in the system. It was found that sulphur dichloride is dissociated to the extent of about 16% into the monochloride and chlorine at the ordinary temperature.

Lowry was in the habit of publishing his papers in series with a common general heading and a more distinctive sub-title; in the series headed "Studies of Valency" the general title was indicative of his constant endeavour to apply modern physical conceptions quantitatively to chemical problems rather than to any continuity of subject. Thus, in one of these papers he concluded that hydrogen is capable of co-ordination like most other elements, basing his decision on such considerations as the crystal structure of ice, the existence of the dissociation $KHF_2 \rightleftharpoons \overset{+}{K} + \overset{-}{H}F_2$, in which the complex anion should have the constitution $\overset{-}{F}\overset{+}{H}\overset{-}{F}$, and the phenomena of tautomerism. In other papers of the same series he dealt with the constitutions of thallium and tellurium compounds; he resolved phenyl-*p*-tolylmethyltelluronium iodide into its optically active components by means of the camphorsulphonic acids and showed that the dextro- and the lævo-rotatory iodide undergo very rapid racemisation in acetone and ethyl acetate solutions.

During the last few years Lowry was engaged on the experimental study of the binary systems, N_2O_3–H_2O and N_2O_4–H_2O, with a view to completing the triangular phase diagram for the ternary system, H_2O–N_2O_3–N_2O_5. In the course of this difficult piece of work it was observed that on passing nitrogen peroxide into ozonised oxygen a blue gas, probaby NO_3, is produced; the gaseous mixture ignites below 100°, showing a deep blue wave-front. This curious example of combustion is probably represented by the equation $NO_3 + O_3 = NO_2 + 2O_2$.

Lowry found ample opportunity for the exercise of his gift of attracting collaborators in his work when appointed in 1920 to organise the new laboratory of physical chemistry in Cambridge. Here his ability as an organiser and his faculty for arousing enthusiasm were given full scope; the result is seen in the large number of important experimental papers published by Lowry and his co-workers during his sixteen years as Professor of Physical Chemistry. Few science laboratories in the country have risen to such high rank as creative institutions in so brief a period.

As a master of organic technique and theory Lowry possessed an advantage denied to many physical chemists; he had a vast detailed knowledge of those branches of science which he had made his own, and this information was freely at the service of others. He was an indefatigable worker and his pertinacity was shown in the way in which he returned over and over again to some earlier subject of investigation as new modes of elucidating a problem occurred to him. Whilst he discussed freely any subject which he understood, he was too honest to advance opinions on matters of which he was ignorant and did not always realise that others might not be so reticent. A bright idea, such as a qualitative application to chemistry of a quantitative physical conception, could always capture his attention, but his instinct for exact measurement quickly brought him back to earth. To Lowry scientific theory existed as a means of correlating the facts and though tenacious of his views he would replace them readily by others which fitted better.

Lowry had been an active member of the Faraday Society since its foundation in 1903 and played a leading part in its discussions, acting as its President in 1928—1930. As a firm believer in the stimulating effect of exchange of ideas between men of similar general interests but of different modes of approach he was often instrumental in attracting foreign specialists to this country, going to great pains to arrange meetings for them and extending to them an ample hospitality.

Lowry acted as Director of Shell-filling from 1917 to 1919; he did valuable service on

the Trench Warfare Committee and the Chemical Warfare Committee and was an associate member of the Ordnance Committee at the time of his death. His war services gained him the C.B.E. and the Italian Order of St. Maurice and St. Lazarus. He took the D.Sc. (London) in 1899 and held the honorary degree of M.A. (Cambridge) and doctorates of science of Dublin and Brussels; he became a Fellow of the Royal Society in 1914.

In addition to some hundreds of important papers published with numerous collaborators, Lowry wrote several useful books; the last of these, on "Optical Rotatory Power," was issued in 1935 and will long remain a standard work on the subject. The immense amount of accurate experimental work which Lowry has left on record secures him a permanent place in the history of the science to which he was devoted. His old colleagues and students in the laboratory of physical chemistry which he built up at Cambridge will remember him as a staunch friend, an inspiring teacher and an indefatigable worker who has passed too soon from their ranks. W. J. POPE.

CAMILLE MATIGNON.

1867—1934.

ARTHÈME CAMILLE MATIGNON was born on January 3rd, 1867, at Saint Maurice-aux-Riches-Hommes, a little village in the Department of the Yonne in Burgundy; he died suddenly in Paris on March 18th, 1934. He was educated first at the school of St. François de Salles at Troyes and at the Lycée Condorcet at Paris, whence he passed to the Ecole Normale in 1886; after a brilliant career as a student he took his licentiate in mathematics and the physical sciences in 1888 and his final examinations in the physical sciences in 1889. Berthelot then appointed him an assistant at the Collège de France, and in this capacity Matignon carried out a number of pieces of work, chiefly of a thermochemical nature, which gained for him his doctorate. In 1893 Matignon was appointed a lecturer in the University of Lille and in 1894 became also Director of bleaching, dyeing and finishing at the Institut industriel du Nord; in 1898 he was appointed a lecturer at the Sorbonne and an Assistant Professor at the Collège de France, becoming an auxiliary Professor in 1903. When Le Chatelier succeeded Moissan at the Sorbonne in 1908 Matignon was elected to the Chair of Inorganic Chemistry at the Collège de France and held this position until his death. He was decorated as a Chevalier of the Légion d'Honneur in 1908 and was elected a member of the Académie des Sciences in succession to Haller in 1926; he was President of the French Chemical Society in 1932 and had acted as chief editor of *Chimie et Industrie* since the establishment of this journal in June, 1918, under the auspices of the French Society of Chemical Industry. He was elected an honorary Fellow of the Chemical Society on November 2nd, 1933.

In his early work with Berthelot, Matignon made an extensive study of the heats of combustion of the more important gaseous hydrocarbons and followed this by determinations of the heats of formation of ethyl alcohol, formic and acetic acids, and of a large number of sugars and related compounds. These investigations, carried out with the aid of Berthelot's calorimetric bomb, entailed much careful work in the preparation of highly purified materials and in the analysis of the products of combustion. Matignon then conceived the ambitious project of working out the energy relations subsisting between the closely related members of some one large group of organic compounds; he chose for this purpose a set of about seventy derivatives of urea, many of which were new, and studied their heats of formation, hydrolysis and interconversion. The results of this extensive piece of experimental work led him to confirm Murdoch and Doebner's view that hydurilic acid is the diureide of ethanetetracarboxylic acid; he also concluded that allantoin is the corresponding derivative of dihydroxyethanetetracarboxylic acid, a view now abandoned in favour of the half-acetal constitution advanced later by Piloty and others. In the course of this work Matignon drew attention to a number of thermochemical regularities, such, for instance, as that the replacement of hydrogen attached to nitrogen by an alkyl radical leads to a greater increase of the heat of combustion than when the replaced atom is directly

joined to a carbon atom; the application of this rule led him to confirm Grimaux's conclusion that his "pyvuril" is 5-methylallantoin. The rule was extended later to embrace the fact that nitric esters are more powerful explosives than nitro-derivatives. Matignon's thermal studies of urea derivatives were in part prompted by the desire to elucidate the important part played in the living organism by the changes which these substances undergo; he was the first to apply thermochemical data to the interpretation of reactions in which the formation and hydrolysis of such compounds are involved. He was thus able to foresee that formic acid and urea should react at the ordinary temperature to yield formylurea and to show experimentally that the condensation proceeds as a reversible reaction; a study of the hydrolysis of parabanic, oxaluric and dimethylparabanic acids by water and by alkalis showed these also to proceed as balanced reactions and indicated the probability that equilibria of the type established are operative in vital processes. Incidentally to this work a number of salts of urea with weak acids, such as acetic and glycollic, were prepared and shown to be completely hydrolysed by water in the cold; the several types of acidic function exhibited by such compounds as hydurilic and oxaluric acids were also elucidated.

After his return to the Collège de France in 1898 Matignon addressed himself to more fundamental thermochemical questions and more particularly to the thermodynamics of chemical systems. His examination of the part played by heat in chemical reactions led him to the statement of an empirical law of thermodynamics which Nernst termed the "Le Chatelier–Matignon rule." This states that for gaseous equilibria in which one gaseous and one or more solid phases are concerned, such as the sublimation of solids, the dissociation of calcium carbonate, and the like, the relation $Q/T = 32$ holds approximately in all cases, Q being the heat evolved at constant pressure and T the absolute temperature at which the gaseous pressure attains one atmosphere. This empirical law is an extension to chemical dissociation and reaction of Trouton's law concerning heats of vaporisation. The Le Chatelier–Matignon rule can be stated in several ways and may be used to foretell whether certain hypothetical reactions can take place and, if so, whether they are reversible or not; a few of the many previously unknown reactions which were thus predicted and afterwards experimentally verified may be here stated:

(1) The following reactions are reversible: $2KCl + Pt + 2Cl_2 = K_2PtCl_6$ and $2K_4Fe(CN)_6 + Cl_2 = K_3Fe(CN)_6 + 2KCl$. (2) Calcium carbide can absorb nitrogen; this was afterwards verified by Erlvein, who thus obtained calcium cyanamide. (3) Gaseous hydrogen sulphide acts upon potassium carbonate but not on the sodium salt. (4) Sodium chloride reacts with sodium hydrogen sulphate because the normal dissociation pressure accords with the relation $Q/T = 32$. (5) In the reaction $BaO + \frac{1}{2}O_2 = BaO_2 + K$, K should have a value of about 18 instead of 12 as previously recorded; the value was found later to be 19. (6) Oxalic acid acts on sodium chloride, liberating hydrogen chloride. (7) Potassium iodide should absorb oxygen; Basset and Dodé showed in 1934 that this reaction occurs at high temperatures and pressures, yielding potassium iodate. (8) Arsenious anhydride and sodium nitrite should absorb oxygen in accordance with the equations

$$As_2O_3 + O_2 = As_2O_5 + 62{\cdot}6\ K \text{ and } 2NaNO_2 + O_2 = 2NaNO_3 + 45\ K;$$

Matignon and his co-workers showed that these reactions proceed at high temperatures and pressures.

The fact that non-volatile acids, bases and salts will react completely with non-volatile salts if one of the possible products is volatile under the prevailing conditions, was established by Berthollet about 1800; Matignon showed this to be a special case of what he termed the "law of volatility in chemical reactions," which is of general application. The law may be stated as follows: A temperature exists at which reaction will occur in any system of non-volatile liquid or solid substances if that reaction can yield volatile products. This law was verified in a number of cases, notably in those represented by the equations

$$3MgO + 2Al = Al_2O_3 + 3Mg(\text{vap.}) - 172{\cdot}3\ K \text{ and } 3BaO + Si = BaSiO_3 + 2Ba - 37\ K.$$

Both reactions proceed to completion and the second, in which ferrosilicon is heated with baryta in a steel tube at 1200°, might be used economically for the manufacture of barium.

C Matignon

[To face p. 706.

The law of volatility explains why, although carbon monoxide has a low heat of formation, carbon finds such wide applications as a reducing agent.

Whilst at the Sorbonne, Matignon carried out a great deal of work on the metals of the rare earths. By heating a mixture of the oxide of the metal with magnesium so as to liberate the rare-earth metal in nitrogen and in hydrogen, he showed that nitrogen combines rapidly with thorium, cerium, lanthanum, praseodymium, neodymium, samarium, gadolinium, ytterbium and yttrium and that hydrogen is rapidly absorbed by the last six of these metals. In collaboration with Delépine he prepared anhydrous thorium chloride by heating thoria in carbon tetrachloride vapour, reduced it to the metal by sodium, and prepared the hydride, ThH_4, and nitride, Th_3N_4. With Burion he worked out a general method for the preparation of such anhydrous chlorides as those of thorium, silicon, aluminium, vanadium, praseodymium, neodymium, samarium, vanadium, chromium, etc., based on the action of sulphur chloride and chlorine simultaneously on the corresponding oxides. This method of preparation proved very convenient and facilitated the production of large quantities of the rarer anhydrous chlorides. These were used for the determination of the physical and more particularly of the thermal constants of the salts and for the preparation of compounds which served to illustrate and extend Matignon's work on energetics. Thus he showed that seven compounds of neodymium chloride, $NdCl_3$, and eight of samarium chloride, $SmCl_3$, with ammonia exist, each stable within certain temperature limits at atmospheric pressure; a compound in which samarium acts as a bivalent element, namely, the chloride, $SmCl_2$, was obtained by the action of hydrogen or ammonia on the perchloride, $SmCl_3$. The fact that samarium can act as a bivalent element was confirmed by the preparation of the iodide, SmI_2; later Urbain and Burion obtained the compound $EuCl_2$, and Klemm and Shuth, $YbCl_2$, and it now appears that samarium, europium and ytterbium alone among the metals of the rare earths can exhibit bivalency. A large proportion of the available physical and thermal data concerning the elements of the rare earths were provided by this chapter of Matignon's activities.

Matignon showed that all technical samples of zinc dust contain nitrogen, in general, 0·2—0·4%, but that nitrogen is not absorbed by zinc between its melting and boiling points; commercial aluminium and ferromanganese also contain nitrogen. In general the metallic nitrides are more stable than the oxides towards heat; the consequence was drawn that nitrides which are unattacked by oxygen at high temperatures, such as those of silicon and aluminium, were formed during the cooling of the earth and later yielded ammonia, assimilable by plant life, by the action of water. In collaboration with Lassieur, Matignon showed that zinc begins to combine with oxygen at 600° and with nitrogen at 670°; they prepared the pure crystalline nitride, Mg_3N_4, and showed it to have a higher heat of formation than lead oxide.

During the War the shortage of sulphuric acid led Matignon and Meyer to study the ternary system, water–sodium sulphate–ammonium sulphate, with a view to utilising sodium bisulphate for the large-scale manufacture of ammonium sulphate. The need for nitrogenous manures also led to the study of the equilibrium between ammonium carbonate and urea; during this work, carried out with Fréjacques, it was found that urea, which begins to decompose at its melting point, 132°, is stable at temperatures above 150° in the presence of ammonia. Amongst war activities it may be noted that Matignon discovered an iron–alumina catalyst to be the most efficient in the ammonia synthesis, that he devised a scheme for utilising the oxidation reaction, nitric acid–nitrous acid, for carrying out oxidation reactions on a technical scale and applied it to converting a cargo of sugar, spoilt by sea-water, into oxalic acid, the nitric acid being regenerated by air oxidation from the nitrous fumes.

Matignon was fertile in expedient and his papers reveal many ingenious laboratory devices. He prepared monosodioacetylene, NaC_2H, which is formed below 190°, and the disodio-derivative, produced above 210°, in a pure state by the action of the gas on sodium under conditions which prevented local superheating and showed that the monosodio-derivative decomposes quantitatively into disodioacetylene and acetylene at 210°. For the desiccation of gases he introduced the use of fused common salt ground up with metallic sodium, and he obtained hydrogen phosphide, containing a little hydrogen as the only

impurity, by utilising the mixture of calcium and aluminium phosphides produced by the interaction of calcium phosphate and aluminium powder. During the War he studied many waste products, such as the marc or grape refuse and the vinasse from brandy distillation residues, with a view to their economic utilisation; in this connexion his association with the late Paul Kestner was a very happy one. He was an ardent apostle of intensive agriculture and applied much of his scientific and literary talent to supporting the thesis that the prime need of agricultural France was more artificial manure provided by more intense scientific effort and made available by more efficient industrial organisation. His campaign in this field had much success, though naturally less immediately than he would have wished; it is too soon to appraise at its true value the service which Matignon rendered to his country by laboratory work, writings, and the spoken word on the subject of scientific agriculture.

Those of his English colleagues who had the honour of attending the bicentenary of the birth of Priestley celebrated by the French Chemical Society in 1933 and heard the address which Matignon delivered on the life and work of the discoverer of oxygen recognised that they were listening not only to an orator but also to one who took a real delight in historical studies; the discourse was not of mere ephemeral interest but will remain as a substantial contribution to the history of early chemical research. The scientific knowledge of the ancients, as, for example, the agricultural wisdom displayed by Virgil in the "Georgics," roused Matignon to enthusiasm; his interest in the past and in the history of his own country of Burgundy led to his election as President of the Société Archéologique de Sens in 1932 and of the Congress called at Avallon in 1933 to celebrate the tercentenary of Vauban.

Matignon was an eloquent speaker and wrote in a lucid, convincing style. The editorials which he contributed monthly to *Chimie et Industrie* from 1918 to the end of his life were read with interest by the whole chemical world; the last of these—on the fiftieth anniversary of the death of Dumas—was published a few days after his own death. Matignon's striking personality and his gay, vivacious enthusiasm made him a notable figure. He did much to promote the re-establishment of those normal relations between scientific men which had been so rudely shattered by the Great War; he had many friends far outside his own country who will remember him with affection and respect. W. J. POPE.

JULIUS ARTHUR NIEUWLAND.

1878—1936.

THE sudden death of the Rev. Julius Arthur Nieuwland, C.S.C., Professor of Organic Chemistry at Notre Dame University, which occurred on June 11th, 1936, ended a life full of interest in science and rich in accomplishments.

Born at Hansbeke, near Ghent, Belgium, on February 14th, 1878, and taken to South Bend, Indiana, when he was about three years of age, Nieuwland grew up in this American Middle Western city, where his parents had settled. There he attended a parochial school, was graduated from the University of Notre Dame in 1899, and ordained priest in the Congregation of the Holy Cross in 1903. The sciences that interested him most were botany and chemistry. In 1904 he obtained the Ph.D. degree from Catholic University, Washington, D.C., the subject of his thesis being "Some Reactions of Acetylene."

Thereafter he taught botany at the University of Notre Dame for fourteen years and organic chemistry from 1918 until his death. His interest in botany was lifelong. Much of his time was devoted to field excursions and the classification of higher plants. He founded and edited the *American Midland Naturalist*, a journal devoted primarily to the natural history of the prairie states, and prepared an "Outline of Plant Organography and Terminology."

His chemical researches continued along the lines begun by his thesis. He was the first to use copper as a catalyst for acetylene reactions and prepared divinylacetylene, a compound formed by the chemical union of three molecules of acetylene. Later, the possibilities

of monovinylacetylene, which he also obtained, without isolating or identifying it, were recognised and formed the basis of further work leading to chloroprene and finally to its product of polymerisation, the artificial rubber "DuPrene." These investigations, an outgrowth of a purely theoretical study of acetylene reactions, were carried out in the laboratories of the DuPont Company, with whom Father Nieuwland collaborated.

His acetylene researches also formed the basis for the development of lewisite under the direction of Professor G. N. Lewis of the University of California.

Father Nieuwland, or Dr. Nieuwland as he preferred to be called, was a member of the American Chemical Society, the Chemical Society, London, the German Chemical Society, the American Association for the Advancement of Science, the Biological Society of Washington, the Washington Academy of Science, and the Indiana Academy of Science, of which he was president in 1934. He was honoured for his work in chemistry by awards of several medals, such as the Gold Medal of the American Institute and the Nichols Medal, presented by the New York Section of the A.C.S. in 1935.

Nieuwland was a very modest man, respected and loved by all who knew him. Through his death science has lost a capable investigator and his students and fellow workers a valued adviser.

W. S. CALCOTT.

P. A. ELLIS RICHARDS.

1868—1936.

By the passing on the 22nd of December last of Percy Andrew Ellis Richards, at the age of 68, chemistry lost one of its most devoted servants and this Society one who throughout a long period as a Fellow held it in high regard.

Born in 1868 and educated at St. Paul's School and King's College, London, he studied analytical chemistry under the late Professor C. W. Heaton, whom he succeeded in the post of lecturer in chemistry and physics at Charing Cross Hospital. On the death of his chief he set up in practice as consulting and analytical chemist. Soon afterwards he was appointed public analyst for the parish of St. Martin-in-the-Fields, and, when his parish and others were united to form the City of Westminster, continued as one of the three public analysts for the City. He was appointed to a similar post at Hammersmith in 1904 and for many years acted as honorary analyst to Charing Cross Hospital. His experience and ability in medical chemistry and toxicology were drawn upon in his work in connexion with some famous cases.

Richards was a loyal and active Fellow of the Institute of Chemistry, serving on the Council for two periods of four years, as auditor for four years, and as examiner in Branch E for a further four-year period. He served the Society of Public Analysts for seventeen years as honorary secretary and was then elected to the presidential chair, an honour which he carried with distinction.

During the many years he was in practice he carried out work for the Local Government Board—now the Ministry of Health—upon the "facing" of rice, upon preservatives in imported meat, and upon vinegar, the results of which are embodied in official communications. He also served on two Departmental Committees appointed by the Minister of Health; the first of these was on preservatives and colouring matters in food and the second on "improvers" in flour. In 1906 he was a member of the Joint Advisory Committee of the Society of Public Analysts and the Pharmaceutical Society which had the subject of drugs under consideration and to this Committee he acted as honorary secretary.

A public analyst of distinction, Richards was no less successful as a teacher. In addition to the post at Charing Cross Hospital, he held that of professor of chemistry at Queen's College, London, and was also lecturer in chemistry and metallurgy at the Royal Dental Hospital. His very many students at these institutions will remember with affection the kindly and gracious teacher who spared no pains in explaining so lucidly all their difficult problems. He wrote for his students at Charing Cross Hospital a small text-book on practical chemistry which he later enlarged to cover a wider syllabus; this

became probably the best-known work on the subject among medical students. He had many private pupils in analytical chemistry who have since successfully established themselves in posts under various Governments, Local Authorities, and in commercial chemical posts. All these, the writer among them, will note his passing with especial regret, for we owe much to the careful and conscientious training he gave us. We were privileged to gain an insight into the working of his mind and into those painstaking methods wherein results were checked and again checked before final acceptance.

His contributions to chemical and medical literature were many and embraced subjects far removed from his own particular sphere of food and drug analysis. Many Fellows of this Society will be conversant with those published in *The Analyst* and there is consequently little need to recount them all here. He was the first to notice the action of weak acids on soluble fluorides and successfully demonstrated that citric and tartaric acids, and even carbon dioxide, caused the liberation of hydrofluoric acid from them and that therefore their use as food preservatives was attended by some danger of injury to health. Up to that time fluorides and fluosilicates were so used, but nowadays are very infrequently encountered. He contributed papers to *The Lancet* and other medical journals upon the saline waters of Salsomaggiore and Boston Spa, upon the determination of platinum in dental alloys, and upon the determination of iron in animal organs. In the last he was associated with Dr. William Hunter in researches on pernicious anæmia, in which disease there is an accumulation of iron in the liver, kidneys and spleen; as his contribution to this work he carried out determinations of iron content in a very large number of cases.

Throughout a busy life Richards found time to serve on various councils and committees at the institutions wherein he taught. He had, too, a marked ability in the field of finance and served very successfully Queen's College as bursar and the Royal Dental Hospital as honorary treasurer. All these additional duties he performed very faithfully and with distinction; there were no adverse balances in Richards' day which wise investment and careful husbanding of resources could counter.

The life now ended began in days when modern chemistry was hardly out of its infancy, when most of the processes which are now commonplace with us were unknown, and when many of the refined instruments we now use were not invented. One may instance the Kjeldahl process for the determination of nitrogen in organic compounds; one of the stories Richards told was of the use of the combustion method for the determination of proteins in milk! Another story had reference to the comparatively massive quantities of material worked upon; for the determination of fat, quantities of the order of 50 grams were taken and the method usually consisted in grinding the dried material with sand and ether in a mortar, the fat being finally recovered. These and other methods equally crude were current in Richards' early days. He witnessed the introduction of all the refinements we now use; his life may be said to span the period between macroscopic and microscopic analysis, for microanalysis has now been brought to a perfection at once ingenious and beautiful. One might elaborate this theme and quote many examples of almost unbelievable progress. But most of us know the history of our own science and among ourselves there is no necessity to dwell upon it. Richards learnt his organic chemistry at a time when constitutional formulæ were unknown and he never forgot to remind his pupils of the many advantages these and other things brought. For them no lists of compounds of empirical formula CH_2O and so on; for them a nearly completed Periodic Table—no having to memorise precisely where many lacunæ fell. One wonders how he would view the possibility, lately revealed, of our having to extend the table to include elements of our own manufacture, wherein the works of Nature have been excelled by her creature Man; or whether he would feel quite happy in the contemplation of constitutional formulæ for some vitamins.

Richards lived to witness the transition of analytical chemistry from a position almost of contempt to its rightful place of equality with synthetic chemistry, a fact which afforded him keen pleasure, though for the last few years this was tinged with regret that his failing health prevented him taking an active part in this progress. It seemed that fate had laid him by just when, being at the height of his powers, he could have contributed not a little to the progress of our science. During his life he gave much to chemistry; some of us

who knew him well think he might have spared himself a little and thus have escaped that breakdown in health that robbed us of his co-operation. Very few can hope to excel his record, not many even to equal it, but all will honour him for what he gave so freely and ungrudgingly to us and our cause. F. W. EDWARDS.

PERCY RICHARD SANDERS.

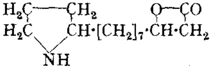
1875—1937.

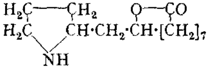
PERCY R. SANDERS was born on March 19th, 1875, and entered the Inland Revenue Service in 1895. He studied at the Royal College of Science, London, from 1896 to 1898 and worked in the Government laboratories before being appointed to take charge of the Customs Chemical Station at the port of Newhaven. He was an enthusiastic Territorial Officer; during the early part of the Great War he was placed in charge of the construction of an extensive scheme for the defence of the Newhaven Port, and was awarded the Military Cross. After the war, he returned to the Customs and Excise Department, in which he served until his death on January 18th last. He maintained his interest in chemistry throughout the whole of his career and earned the esteem of all with whom he came into contact, officially and socially. A. MORE.

140. *Constitution of Carpaine. Part III.*

By G. BARGER, ROBERT ROBINSON, and T. S. WORK.

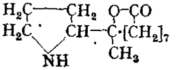
CARPAINE is a lactone and is hydrolysed to carpamic acid (Barger, J., 1910, **97**, 466), from which the original alkaloid has so far not been regenerated. Oxidation with nitric acid yields azelaic acid, proving the presence of a chain of seven methylene groups (Barger, Girardet, and Robinson, *Helv. Chim. Acta*, 1933, **16**, 90). This led to the suggestion that either a β-lactone ring (as in I) or a much larger lactonic ring (as in II) is present.

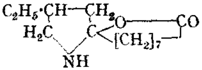
(I.) 

 (II.)

We have now found that carpaine and some of its degradation products contain one *C*-methyl group (estimated by the Kuhn–Roth method). A formula of type (I) and containing such a methyl group could only have six methylene groups between its two rings; this therefore rules out a β-lactone structure, which is also contradicted by the ozonisation of anhydrocarpamic acid (see below). Formula (II) can, however, be readily modified to accommodate a methyl group, since it has a spare carbon atom between the two rings, which we now therefore consider to be joined directly. The large lactone ring also explains our inability to regenerate carpaine from carpamic acid. In assigning a position to the methyl group we take into account the further observation that carpamic acid is a tertiary and not a secondary alcohol. This was already indicated by the observation of Barger, Girardet, and Robinson that carpamic acid, on heating with formaldehyde, merely forms *N*-methylcarpamic acid, whilst pyrrolidylpropanols, containing a secondary alcoholic group, are transformed to ketones (Hess, *Ber.*, 1913, **46**, 4107).

Additional evidence for the tertiary alcohol group is now provided by the observation that on boiling carpamic acid with potassium dichromate and sulphuric acid a considerable proportion is recovered unchanged, and no keto-acid can be isolated. Accordingly we place the methyl group as in (III), which formula is being used as the basis of synthetic experiments (see the succeeding papers).

(III.) 

 (IV.)

The only arrangement in which the tertiary alcohol group does not involve a methyl group is of type (IV), where two carbon atoms have to be accommodated on the pyrrolidine ring; since they cannot both be *C*-methyl groups, this alternative has been illustrated with an ethyl group in an arbitrary position. Neither of the last two carbon atoms can be in the lactone ring, for this would then yield sebacic rather than azelaic acid. We do not consider a formula of type (IV) very likely; (III) is moreover in accordance with a biochemical origin from proline. In all the above formulæ the lactone ring is represented as attached to an α-position of the pyrrolidine ring; the evidence for this is of two kinds. In the first place one of the α-positions must be substituted, for carpamic acid yields no colour reaction with isatin which, according to Grassmann and von Arnim (*Annalen*, 1935, **519**, 192), is given by pyrrolidine derivatives in which both α-positions are free. In the second place the elimination of the nitrogen atom from carpaine results in substances containing 14 carbon atoms which still have only one *C*-methyl group; if the lactone ring were attached in a β-position, a second *C*-methyl would be generated by the opening of the pyrrolidine ring. This opening has been brought about both by violent reduction and by exhaustive methylation. When carpamic acid is heated with hydriodic acid and phosphorus at 320°, the nitrogen is eliminated as ammonia and a *hydrocarbon* results, probably $(CH_2)_n$. From a molecular weight determination and the fact that myristic acid by similar treatment yields tetradecane, without decarboxylation (Krafft, *Ber.*, 1882, **15**, 1700), we believe the hydrocarbon from carpaine to be $C_{14}H_{28}$ or possibly $C_{14}H_{30}$. It contains only one *C*-methyl group. (The formula $C_{14}H_{28}$ would involve the formation of a ring, not readily explained.) The exhaustive methylation of carpaine, followed by catalytic reduction, yielded a lactone, which was hydrolysed to an *acid*, $C_{14}H_{28}O_3$, with one *C*-methyl group. It was characterised as the *p*-phenylphenacyl ester and its synthesis is being attempted.

Whilst the direct dehydration of carpamic acid, with the formation of a double bond, yielded no satisfactory product, this end was achieved indirectly by successive treatment with phosphorus pentachloride and potassium hydroxide. The unsaturated anhydrocarpamic acid so obtained was reduced to *deoxycarpamic acid*, and was also oxidised by ozone and by permanganate. The ozonisation product, obtained in minute amount, was an acid with an equivalent weight corresponding to $CH_3·CO·[CH_2]_7·CO_2H$, in any case monobasic. Formula (I) would require the formation of oxalic or malonic acid and an amphoteric substance. Oxidation of anhydrocarpamic acid with permanganate yielded azelaic and other acids.

Experimental.

The carpaine used in these experiments was obtained from 100 kg. of dried old leaves of *Carica Papaya*, which were extracted with 80% alcohol containing 0·5% of acetic acid. The yield (0·018%) was extremely disappointing; young leaves contain very much more alkaloid.

C-Methyl groups in carpamic acid were estimated by the Kuhn–Roth chromic acid method by Dr. H. Roth (Found: 0·99, 1·00, 1·01, 1·02).

Oxidation of Carpamic Acid by Chromic Acid.—Carpamic acid hydrochloride (0·8 g.) was dissolved in water, and the calculated quantity of potassium dichromate in sulphuric acid (Beckmann's mixture) added; after heating for 1 hour, the dichromate had been used up. After removal of inorganic matter an oil was obtained, a solution of which in the minimum quantity of hydrochloric acid yielded crystals on evaporation; these, recrystallised from acetone, had m. p. 157—158°, and m. p. 160° when mixed with carpamic acid hydrochloride; 40% of the starting material was thus recovered unchanged. The small amount of residual uncrystallisable oil gave no reactions for a ketone.

Reduction of Carpamic Acid.—Carpamic acid hydrochloride (0·5 g.), red phosphorus (0·5 g.), and hydriodic acid (5·0 g., *d* 1·7) were heated for 7 hours at 320—330°. After dilution with water and extraction with ether, the ethereal solution was freed from iodine with copper powder. On evaporation an oil was left, which distilled in a high vacuum at about 90° and remained liquid. Yield, 30—80 mg. (Found: C, 86·0; H, 13·9; *M*, by micro-Rast, 192, 185. $C_{14}H_{28}$ requires C, 85·7; H, 14·3%; *M*, 196). Myristic acid, treated in the same way, yielded a very similar *hydrocarbon* (Found: C, 84·6; H, 15·5. $C_{14}H_{30}$ requires C, 84·8; H, 15·2%). The refractive indices, kindly determined by Dr. E. G. V. Percival, were $n_D^{17°}$ 1·4325 for the hydrocarbon from carpaine and 1·4320 for that from myristic acid. The *C*-methyl found in the hydrocarbon from carpaine was 0·93, 0·88 (by Dr. H. Roth). In the aqueous solution, which was extracted with ether, ammonia was recognised by Nessler's reagent.

Exhaustive Methylation.—Carpaine (4 g.) was dissolved in methyl alcohol and heated at 100° for 12 hours with excess of methyl iodide. The quaternary iodide was decomposed with silver carbonate, and the ether-soluble portion of the resulting oil treated again with methyl iodide in the same way. The quaternary carbonate was heated at 150° in a high vacuum until frothing ceased, and then distilled (bath 160—180°). The colourless oily distillate was heated with methyl iodide for 16 hours at 100°, and the carbonate distilled (bath 160—190°). The distillate (2·1 g.) was reduced catalytically with platinum oxide and hydrogen, and the resulting oil separated into a neutral (0·45 g.) and a basic fraction (1·0 g.), both soluble in ether. The latter, treated as before, yielded a further 0·05 g. of neutral oil. The total (0·5 g.) was boiled with alcoholic potassium hydroxide for 4 hours. On acidification and extraction with ether a crystalline acid was obtained, melting indefinitely at 20—25° (Found: C, 69·0; H, 11·2; equiv. by titration, 249. $C_{14}H_{28}O_3$ requires C, 68·9; H, 11·5%; equiv., 244). The acid contains one C-methyl group (Found: 0·35 by Dr. H. Roth, who suggests that in an open vessel some methyl *n*-butyl ketone escapes unoxidised. Myristic acid gave a negative result). The *hydroxyisomyristic acid* yielded a crystalline *p*-phenylphenacyl ester.

Attempted Direct Dehydration of Carpamic Acid.—The acid was recovered in almost quantitative yield after heating at 170° for 10 hours with concentrated sulphuric and glacial acetic acids (2 : 1). Treatment with zinc chloride in acetic acid yielded an uncrystallisable oil.

Chlorination of Ethyl N-*Methylcarpamate.*—This ester (0·5 g.) (Barger, Girardet, and Robinson) was dissolved in ether and treated with slightly more than the theoretical quantity of thionyl chloride. After standing overnight, the ethereal solution was washed with aqueous sodium carbonate, and the oil, left on evaporation, was distilled in a high vacuum. The distillate (0·2 g.) set to a crystalline mass melting rather indefinitely at about 30° (Found: Cl, 12·0. $C_{17}H_{32}O_2NCl$ requires Cl, 11·2%).

Indirect Dehydration of Carpamic Acid. Anhydrocarpamic and Deoxycarpamic Acids.—Carpamic acid hydrochloride (1·0 g.) was dissolved in the minimum quantity of phosphorus oxychloride and excess of the pentachloride was added. After heating for 2 hours on the water-bath the oxychloride was removed in a vacuum. The residue was boiled for 4 hours with 25% potassium hydroxide in methanol, cooled, made just acid to methyl-red, evaporated to dryness, and extracted with alcohol. Anhydrocarpamic acid was obtained as a non-crystallisable oil and was reduced with platinum oxide in acetic acid; 61 c.c. of hydrogen were absorbed (calc. for 1·0 g. of carpamic acid hydrochloride, 80 c.c.). The *deoxycarpamic acid* crystallised on evaporation; after recrystallisation from acetone–alcohol, it sublimed at 155—160°/1 mm. in needles, m. p. 181°; yield, 200 mg. (Found: C, 69·9; H, 11·4; N, 5·2. $C_{14}H_{27}O_2N$ requires C, 69·7; H, 11·2; N, 5·8%). The solubilities were similar to those of carpamic acid.

Ozonisation of Anhydrocarpamic Acid.—The crude anhydrocarpamic acid, prepared as above from carpamic acid (0·5 g.), was ozonised in aqueous solution. After acidification and extraction with ether the residual acidic oil distilled in a high vacuum (bath 130—140°). The colourless distillate did not crystallise (Found: equiv. by titration, 190. A keto-acid, $CH_3{\cdot}CO{\cdot}[CH_2]_7{\cdot}CO_2H$ requires equiv., 186). After esterification with diazomethane and treatment with ammonia a crystalline substance was obtained in amount too small for further examination.

Oxidation of Anhydrocarpamic Acid with Permanganate.—The crude anhydro-acid from 0·9 g. of carpamic acid hydrochloride was treated in slightly alkaline aqueous solution with 2% potassium permanganate solution; 78 c.c. were decolorised in the cold, and a further 72 c.c. in the course of 2 hours on the water-bath (total, 3·1 oxygen atoms). The solution was filtered, acidified, and extracted with ether. The ethereal extract (*A*) and the acid solution (*B*) were evaporated to dryness. (*A*) yielded an oil, which on distillation at 1 mm. gave (1) a semi-solid mass (bath at 170—190°), m. p. 110—124°, very sparingly soluble in ether; the amount was insufficient for purification (? impure suberic acid; cf. Barger, Girardet, and Robinson); (2) a crystalline solid (bath 190—210°). After five crystallisations from water the m. p. was constant at 103—104° and the mixture with authentic azelaic acid (m. p. 105—106°) melted at 103—104·5°. The quantity was insufficient for analysis. The residue from (*B*) was separated from inorganic matter by extraction with alcohol and distilled at 1 mm. (bath 150—180°). A colourless nitrogen-free oil was obtained, soluble in water, sparingly in ether, and acidic. On treatment with ammonia and distillation with zinc dust the pyrrole reaction with pine wood was obtained (succinic acid ?).

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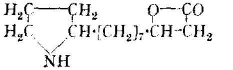
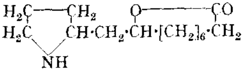
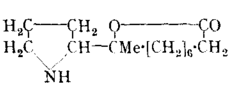
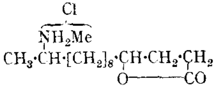
141. *Synthetical Experiments relating to Carpaine. Part I. Synthesis of a Basic Long-chain Lactone.*

By G. BARGER, ROBERT ROBINSON, and Y. URUSHIBARA.

ACCORDING to Barger, Girardet, and Robinson (*Helv. Chim. Acta*, 1933, **16**, 90), carpaine might be (I) or (II); more recently, formulæ such as (III) have come into consideration.

(I.)   (II.)

(III.)   (IV.)

In any case, carpaine is certainly the lactone of a hydroxyimino-acid (carpamic acid) of the fatty series and it was of interest to prepare such a compound in order to examine its properties.

The starting point was 4-keto-Δ^{13}-tetradecenoic acid, $CH_2{:}CH{\cdot}[CH_2]_8{\cdot}CO{\cdot}[CH_2]_2{\cdot}CO_2H$, which was prepared by the method of G. M. Robinson (J., 1930, 749) and treated with hydrogen bromide in toluene solution with the formation of a homogeneous product. This proved to be the sec.-*bromide*, $CH_3{\cdot}CHBr{\cdot}[CH_2]_8{\cdot}CO{\cdot}[CH_2]_2{\cdot}CO_2H$, because, after replacement of the bromine by hydroxyl and oxidation by means of chromic acid, it afforded 4 : 13-*diketotetradecoic acid*, $CH_3{\cdot}CO{\cdot}[CH_2]_8{\cdot}CO{\cdot}[CH_2]_2{\cdot}CO_2H$. Interaction of the above bromo-acid with methylamine gave 13-methylamino-4-ketotetradecoic acid, which was isolated in the form of a *hydrochloride*, $CH_3{\cdot}CH(NH_2MeCl){\cdot}[CH_2]_8{\cdot}CO{\cdot}[CH_2]_2{\cdot}CO_2H$. On reduction with sodium amalgam, the corresponding *hydroxy-acid* was obtained, and this passed into the *lactone salt* (IV) in hydrochloric acid solution.

One very interesting point of analogy with carpamic acid and carpaine was noted. Carpamic acid and the synthetical hydroxy-acid are tasteless, whereas carpaine and the lactone (IV) are intensely bitter.

Attempts to apply Löffler's *N*-methylpyrrolidine synthesis (*Ber.*, 1909, **42**, 3427, 3431) to the methylamino-acids were unsuccessful.

EXPERIMENTAL.

13-*Bromo-4-ketotetradecoic Acid*.—A solution and suspension of ketotetradecenoic acid in twice its weight of dry toluene was saturated with hydrogen bromide at 0°. After a few hours the excess of hydrogen bromide was eliminated by heating on the steam-bath, and the solvent distilled, finally under diminished pressure. The residue crystallised on cooling and separated from light petroleum in voluminous threads, which shrank on drying, m. p. 56° after sintering at 53° (Found: C, 52·9; H, 7·8; Br, 24·2. $C_{14}H_{25}O_3Br$ requires C, 52·3; H, 7·9; Br, 24·9%). The *substance* is freely soluble in acetone or benzene, and readily soluble in hot light petroleum, much more sparingly so in the cold solvent. The yield was almost theoretical and the whole product had f. p. 53·5° and thus appeared to be homogeneous.

4 : 13-*Diketotetradecoic Acid*.—Bromoketotetradecoic acid (6·4 g.) was neutralised by *N*-sodium hydroxide, and the solution mixed with an excess of freshly precipitated silver hydroxide and heated on the steam-bath. After addition of *N*-sodium hydroxide (20 c.c.), the filtered solution was acidified, the precipitated acid taken up in benzene, and the dried solution concentrated; the *hydroxy-acid* precipitated by means of light petroleum crystallised from benzene in small prisms, m. p. 63—64° (Found: C, 65·2; H, 10·3. $C_{14}H_{26}O_4$ requires C, 65·1; H, 10·1%). This acid gives the iodoform reaction. Its constitution was confirmed by oxidation to a diketone.

A mixture of the hydroxy-acid (1 g.), acetic acid (20 c.c.), and chromic anhydride (1 g.) was kept for 2—3 days and then gently heated. The precipitate thrown down on the addition of water was collected, dried, and twice crystallised from benzene, forming microscopic needles,

m. p. 95·5° (Found : C, 65·5; H, 9·4. $C_{14}H_{24}O_4$ requires C, 65·6; H, 9·4%). The *acid* does not reduce ammoniacal silver solutions, but in the presence of sodium hydroxide a silver mirror is obtained. This does not denote an aldehyde, because the hydroxy-acid exhibits the same behaviour.

13-*Methylamino-4-ketotetradecoic Acid Hydrochloride*.—A solution of bromoketotetradecoic acid (6·4 g.) in a large excess of alcoholic methylamine (33%) was heated at 100° in a sealed tube for 6 hours and then concentrated to a syrup. In later operations, the details of which are probably unnecessarily complicated, we removed unchanged bromo-acid by extraction from an acid solution, rendered the free amino-acid to ether, and eventually prepared the *hydrochloride*. The solution of this salt was evaporated to dryness on the steam-bath, and the residue crystallised from acetone (Found : C, 58·3; H, 9·7; N, 4·5; Cl, 11·6. $C_{15}H_{29}O_3N,HCl$ requires C, 58·5; H, 9·8; N, 4·6; Cl, 11·5%).

13-*Methylamino-4-hydroxytetradecoic Acid*.—Methylaminoketotetradecoic acid hydrochloride was reduced in aqueous solution by means of an excess of 3% sodium amalgam on the steam-bath for 3 hours. The solution was acidified with hydrochloric acid and evaporated to dryness, and the product isolated by extraction of the residue with acetone. The crude substance obtained on removal of the solvent could not be crystallised; it was treated in aqueous solution with freshly precipitated silver carbonate, hydrogen sulphide passed into the filtered solution, and the liquid again filtered and evaporated to dryness. The residue crystallised from alcohol and was then colourless, m. p. 153° (Found : C, 65·8; H, 11·3; N, 5·0. $C_{15}H_{31}O_3N$ requires C, 65·9; H, 11·4; N, 5·1%). This *amino-acid* is readily soluble in water and alcohol, sparingly soluble in acetone and ether, and is tasteless. When it is suspended in water and a few drops of 1% hydrochloric acid, the solution formed is tasteless; in a few seconds a bitter taste becomes apparent and after heating and cooling the solution is intensely bitter; this proves that the hydrochloride of the hydroxy-acid is not bitter.

For the preparation of the substance it suffices to heat 13-bromo-4-ketotetradecoic acid with 33% alcoholic methylamine in a pressure bottle at 100°, acidify the product with hydrobromic acid, remove unchanged acid with ether, neutralise the aqueous solution with sodium hydroxide, and reduce the keto-acid at 100° with 3% sodium amalgam, carbon dioxide being passed through the liquid. The liquid is then neutralised with hydrobromic acid and evaporated, the residue extracted with acetone, and the crude product treated with silver carbonate as already mentioned.

The hydroxy-acid (2·698 g.), dried at 110°, was dissolved in the calculated volume of *N*-hydrochloric acid, and the solution evaporated to dryness. The solid product weighed 2·943 g. (theo. wt., 3·058 g. for simple salt formation and 2·880 g. for lactone formation). When heated with acetic anhydride at 100°, the substance formed an acetyl derivative insoluble in aqueous sodium carbonate and hence was probably the lactone (IV). The salt is intensely bitter.

The *hydrobromide* was soluble in chloroform and on the addition of a few drops of light petroleum separated as an oil that crystallised on keeping at 0°. The colourless plates were hydrated and exhibited no sharp m. p. (Found in material dried at 100° in a high vacuum : C, 53·9; H, 9·1. $C_{15}H_{29}O_2N,HBr$ requires C, 53·6; H, 8·9%).

Attempts to isolate the free lactone failed, as even the mildest methods (such as shaking an aqueous solution with silver carbonate) afforded the hydroxy-acid.

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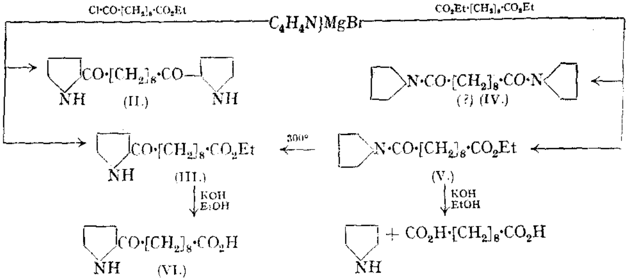
142. *Synthetical Experiments relating to Carpaine. Part II.*

By G. BARGER, ROBERT ROBINSON, and W. F. SHORT.

A SIMPLE test-case for the applicability of Löffler's *N*-alkylpyrrolidine synthesis (*Ber.*, 1909, 42, 3427, 3431) to the long-chain aliphatic series has been examined with unpromising results.

N-*Bromo-*11-*methylaminoundecoic acid*, $NMeBr\cdot[CH_2]_{10}\cdot CO_2H$ (I), has been obtained as an oil and found to suffer extensive decomposition when treated with sulphuric acid. We have therefore devoted attention to the interaction of pyrrylmagnesium bromide with ethyl sebacate and with the ester chloride of sebacic acid with the object of isolating C_{14}-substances

including a normal carbon chain and an α-substituted terminal pyrrole nucleus. The results are summarised below:



The *ester* (III), or an analogue derived from some other dibasic acid, may subsequently become an intermediate in a synthesis of carpamic acid.

These results are not quite what might have been anticipated, since Tschelinzeff and Terentjeff (*Ber.*, 1914, **47**, 2647, 2652) found that pyrrylmagnesium bromide reacted with ethyl acetate, ethyl propionate, and ethyl butyrate with formation of α-pyrryl alkyl ketones in 50—60% yields. Ethyl carbonate, however, afforded ethyl pyrrole-*N*-carboxylate (Tschelinzeff and Karmanov, *J. Russ. Phys. Chem. Soc.*, 1915, **47**, 161, 197).

Experimental.

N-*Bromo*-11-*methylaminoundecoic Acid* (I).—11-Bromoundecoic acid was heated at 100—120° for 5 hours with 33% alcoholic methylamine (10 mols.) as described by Flaschenträger (*Z. physiol. Chem.*, 1930, **192**, 245), but when the alcohol and methylamine were removed by distillation on the steam-bath (finally in a vacuum) and the residue was poured into a large volume of water, a gelatinous precipitate was obtained instead of the crystalline amino-acid. The amino-acid was therefore isolated as its *hydrochloride* by distilling most of the alcohol and methylamine from the reaction mixture, acidifying the remainder with hydrochloric acid, evaporating it to dryness in a vacuum, and extracting the dry residue with boiling acetone. A little methylamine hydrochloride remained undissolved and the filtrate deposited the hydrochloride of the base. This was recrystallised from acetone containing a little water and washed with ether; m. p. 105—105·5° (Found: N, 5·3. $C_{12}H_{25}O_2N,HCl$ requires N, 5·6%. $C_{12}H_{25}O_2N,HCl,H_2O$ requires N, 5·2%). The free amino-acid, liberated by the successive action of silver oxide and hydrogen sulphide, melted at 136—137° as described by Flaschenträger. The yield was 24% and the same yield was obtained when the reaction product was worked up by successive treatment with barium hydroxide, sulphuric acid, silver oxide, and hydrogen sulphide (Flaschenträger reports a yield of 74—76%). Contrary to Flaschenträger's statement, the acid is soluble in dilute aqueous ammonia (also in aqueous methylamine).

An ice-cold suspension of the finely powdered hydrochloride (2·62 g.) in chloroform (20 c.c.) was shaken vigorously with sodium hypobromite solution (2 mols. from 1·6 g. of sodium hydroxide, 15 c.c. of water, and 3·2 g. of bromine). The solid rapidly dissolved and after ½ hour at 0° the chloroform solution was washed with ice-water and dried at 0° over sodium sulphate, and the solvent removed below 30°. A portion of the viscous, light brown oil so obtained was suspended in aqueous potassium iodide, acidified with acetic acid, and titrated with thiosulphate (0·5879 g. required 40·25 c.c. of 0·1*N*-thiosulphate. Found: Br, 27·4. $C_{12}H_{24}O_2NBr$ requires Br, 27·2%). The oil was unstable and in presence of moist solvents rapidly decomposed with regeneration of the amino-acid. Attempts to produce a pyrrolidine by the action of concentrated sulphuric acid at − 15°, 0°, or at room temperature resulted in the liberation of hydrogen bromide and bromine and in carbonisation. A little amino-acid could be recovered from the reaction mixture.

9-Carbethoxynonoyl chloride, $EtO_2C\cdot[CH_2]_8\cdot COCl$, was prepared as described by Robinson and Robinson (*J.*, 1925, **127**, 177). The yield of product, b. p. 175—178°/19—20 mm. or 139°/1 mm., was 96%.

9-2′-Pyrroylnonoic Acid (VI).—Pyrrylmagnesium bromide (prepared from 4·3 g. of pyrrole, 1·54 g. of magnesium, and 7 g. of ethyl bromide in ether) (Oddo, *Gazzetta*, 1909, **39**, 649) was slowly added to an ice-cold solution of 9-carbethoxynonoyl chloride (15·9 g.; 1 mol.) in ether (16 c.c.) in an atmosphere of hydrogen (to prevent rapid aerial oxidation of pyrrylmagnesium bromide). Next day the mixture was heated on the steam-bath for 1 hour. The reaction mixture, which consisted of a thick black tar and an almost colourless, ethereal solution, was shaken with saturated aqueous ammonium chloride and ice until the whole of the black complex had been decomposed and the products passed into the ether. The ethereal solution was washed repeatedly with water and dried over sodium sulphate, the solvent removed, and the residue distilled in a high vacuum (< 1 mm.): (1) Ethyl hydrogen sebacate passed over at 155—175°; (2) a mixture of this ester with ethyl pyrroylnonoate distilled between 175° and 190°; (3) the pyrroylnonoic ester passed over between 190° and 210° and mainly at 190—200°; (4) a small quantity of a solid distilled above 210°. Fractions (2) and (3) were dissolved in ether, repeatedly extracted with dilute sodium carbonate solution and dried, and the solvent evaporated. Recrystallisation of the residue from light petroleum (b. p. 40—60°) by cooling in a freezing mixture afforded long white needles, m. p. 28° (Found: N, 5·1. $C_{16}H_{25}O_3N$ requires N, 5·0%). The yield of this *ethyl 9-2′-pyrroylnonoate* (III) varied from 20% to 55% of the theoretical calculated on the pyrrole employed. Saponification of this ester with 0·5*N*-alcoholic potash afforded the corresponding *acid* and very vigorous treatment with the reagent did not remove the side chain. The acid is very readily soluble in acetic acid, acetone, ether and ethyl acetate, slightly less soluble in benzene and chloroform, considerably less so in methyl alcohol, and almost insoluble in light petroleum. It is best recrystallised from 60% alcohol, from which it separates in small, white, clustered needles, m. p. 85—85·5° (Found: C, 66·9; H, 8·8; N, 5·5. $C_{14}H_{21}O_3N$ requires C, 66·9; H, 8·4; N, 5·6%).

Attempts to prepare a semicarbazone of the ester by the usual method failed and resulted in the production of a green solution; on heating, hydrazodicarbonamide was precipitated.

Reduction of the acid in acetic acid solution in the presence of platinum oxide at 2 atmospheres pressure caused the separation of long white needles (after the absorption of *ca.* 2H). These subsequently dissolved and although 6H were absorbed, the product was entirely resinous. Reduction of the ester with sodium and absolute alcohol produced a bright red, sticky resin.

1 : 8-*Di-2′-pyrroyloctane* (II).—This is the by-product contained in fraction (4) above. It is produced in larger quantity if the 9-carbethoxynonoyl chloride is added to the pyrrylmagnesium bromide. It separates from hot alcoholic solutions in thin, irregular, rhomboidal plates, m. p. 138° (Found: C, 71·9; H, 8·2; N, 9·6. $C_{18}H_{24}O_2N_2$ requires C, 72·0; H, 8·0; N, 9·3%). It is very difficult to free this *substance* from an impurity which gives the pine-splinter reaction when boiled with concentrated aqueous potassium hydroxide, but the pure substance is recovered unchanged after 4 hours' digestion with 5*N*-alcoholic potash. Hence it would appear to be the diketone, but since (i) the carbethoxynonoyl chloride employed in the preparation had a sharp b. p. and was free from sebacyl chloride, and (ii) it was found that ethyl sebacate reacts with pyrrylmagnesium bromide to yield *N*-substituted pyrroles, it may be formed by rearrangement of *N*-(9-2′-pyrroylnonoyl)pyrrole during the distillation.

N-9-*Carbethoxynonoylpyrrole* (V).—Pyrrylmagnesium bromide (from 3·5 g. of magnesium, 16·3 g. of ethyl bromide, 10 g. of pyrrole, and 95 c.c. of ether) was slowly added (ice-cooling, hydrogen atmosphere) to a solution of ethyl sebacate (48·4 g.; 1·25 mols.) in ether (50 c.c.); the mixture was kept for 4 hours and then heated on the steam-bath for 2 hours. The heavy green layer disappeared when the product was shaken with ice and ammonium chloride. The ethereal solution was washed with water and dried, and the solvent removed. A small quantity of pyrrole was recovered by distillation at 20 mm. and the residue was distilled in a high vacuum (< 1 mm.): (1) Ethyl sebacate (30 g.) distilled at 153—160°, followed by (2) a fraction which mostly passed over at 185—190° and (3) a small fraction (*ca.* 1 g.) which solidified immediately in the receiver. Fraction (2) was recrystallised from boiling light petroleum (b. p. 40—60°), a small insoluble portion being identical with the solid obtained from fraction (3). The long, white prisms so obtained had m. p. 43° (Found: C, 68·8; H, 8·9; N, 5·1. $C_{16}H_{25}O_3N$ requires C, 68·8; H, 9·0; N, 5·0%) (yield, 30% on the pyrrole).

Saponification of the *ester* with 5*N*-alcoholic potash afforded an acid which, after recrystallisation from formic acid, melted at 133°, alone or mixed with sebacic acid.

When the ester was boiled gently in an atmosphere of hydrogen, there was no change after the first hour, but between the second and third hour a transformation occurred (probably suddenly) in which three-quarters of the material resinified. Extraction of the residue with light petroleum furnished ethyl 9-2′-pyrroylnonoate, m. p. 28°, which on saponification afforded 9-2′-pyrroyl-

nonoic acid, m. p. 85—85·5° alone or after admixture with the acid prepared by the direct process. Fraction (3) above separated from boiling alcohol in glistening rhombic plates, m. p. 107—107·5°. It yielded pyrrole (intense pine-splinter reaction) when heated with concentrated aqueous potassium hydroxide and so is probably (IV), but it has not been further investigated.

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143. *Synthetical Experiments relating to Carpaine. Part III. Some Derivatives of Tetrahydrofuran and Intermediates of the Aliphatic Series.*

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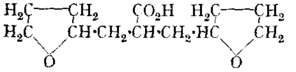
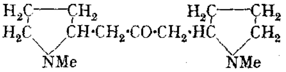
THIS interim report on a research in progress is now submitted because one of us has withdrawn from the investigation and also because the intermediates described may be found of value in other connections.

In view of the accessibility of tetrahydrofurfuryl alcohol experiments have been undertaken with the object of lengthening the side chain and so arriving at possible cyclic ether analogues of carpamic acid or one of its degradation products.

There was good reason to believe that the tetramethylene oxide system could be converted into the pyrrolidine group, relevant observations on the opening of the tetrahydrofuran ring being those of Hamonet (*Ann. Chim.*, 1918, **10**, 24), Paul (*Bull. Soc. chim.*, 1933, **53**, 417), and Starr and Hixon (*J. Amer. Chem. Soc.*, 1934, **56**, 1595) (cf. Hollins, " Synthesis of Nitrogen Ring Compounds," Benn, 1924, pp. 65 *et seq.*).

Tetrahydrofurfuryl chloride (Kirner, *J. Amer. Chem. Soc.*, 1930, **52**, 3251) is surprisingly inert towards such substances as potassium cyanide or ethyl sodioacetoacetate, and even tetrahydrofurfuryl bromide (Dox and Jones, *J. Amer. Chem. Soc.*, 1928, **50**, 2033; Gilman and Brown, *Iowa State Coll. J.*, 1931, **6**, 11; Paul, *loc. cit.*; Robinson and Hart Smith, J., 1936, 196) could not be condensed with the latter reagent in ether, alcohol, dioxan, benzene or toluene as solvent, with or without sodium iodide. Nevertheless, tetrahydrofurfuryl bromide enters into facile reaction with ethyl sodiomalonate in alcoholic solution and *ethyl tetrahydrofurfurylmalonate*, $(C_5H_9O)CH(CO_2Et)_2$, is obtained in good yield. The usual series of processes affords β-tetrahydrofurylpropionic acid, previously obtained by Adams and Kauffman (*J. Amer. Chem. Soc.*, 1923, **45**, 3042) by reduction of furylacrylic acid; the process now described is the more convenient. *Ethyl β-tetrahydrofurylpropionate* is readily reduced by the Bouveault–Blanc method to 3-tetrahydrofurylpropan-1-ol, previously obtained by catalytic reduction of furylacraldehyde (Bray and Adams, *J. Amer. Chem. Soc.*, 1927, **49**, 2105). The alcohol is convertible into *γ-tetrahydrofurylpropyl bromide*, $(C_4H_7O)CH_2{\cdot}CH_2{\cdot}CH_2Br$. Ethyl sodiotetrahydrofurfurylmalonate and tetrahydrofurfuryl bromide afford *ethyl bistetrahydrofurfurylmalonate*, which can be hydrolysed and decarboxylated to *ββ'-bistetrahydrofurylisobutyric acid* (I), a compound structurally related to cuskhygrine (II).

(I.)   (II.)

Although Paul (*Bull. Soc. chim.*, 1935, **55**, 747) has stated that tetrahydrofurfuryl bromide was not transformed into a nitrile by interaction with potassium cyanide at 150°, or in alcoholic solution, we have obtained fair results (47—52%) by prolonged refluxing of an aqueous alcoholic solution of the reactants. An alternative method is to make use of tetrahydrofurfuryl *p*-toluenesulphonate, obtained by Gilman and Brown (*loc. cit.*) as an oil and now crystallised. On hydrolysis of the *nitrile, tetrahydrofurylacetic acid*, $(C_4H_7O)CH_2{\cdot}CO_2H$, is produced and it may be noted that this substance must be prepared in this way because a satisfactory method of preparation of furylacetic acid has not yet come to light.

Details of a highly satisfactory method for the preparation of ethyl 2-furoylacetate are given in the experimental section. We hoped to condense the sodio-derivative of this ester with ω-halogeno-fatty acid esters and to apply similar methods to 2-pyrroylacetic ester. This led to a more prolonged investigation of the aliphatic intermediates than had been anticipated.

Ethyl ω-hydroxy-valerate, -hexoate, and -heptoate are obtainable by a modification of Baeyer and Villiger's process of oxidation of cyclic ketones by means of Caro's acid in the presence of alcohol (*Ber.*, 1899, **32**, 3625; 1900, **33**, 863; Robinson and Hart Smith, this vol., p. 371) and the hydroxyl groups of these esters have been replaced by chlorine and bromine. Careful attention to the conditions is requisite and when hydrogen bromide is used as the reagent there is even some dubiety in regard to the homogeneity of the product. Isomerisation may occur by way of an ethylene derivative and with this in mind we carried out the reaction in the case of ethyl 6-hydroxyhexoate in the presence of oxygen and a " peroxide " catalyst. This should have prevented isomerisation by the mechanism contemplated, because the olefin group would add the bromine terminally if it were formed (cf. Ashton and J. C. Smith, J., 1934, 435, 1308). In point of fact the ethyl bromoheptoate obtained in this way had a higher b. p. than that produced without this precaution and, as the primary bromide ought to have a higher b. p. than the secondary, we think that this and all similar reactions should be effected in the presence of oxygen and peroxide catalysts in order to obtain a homogeneous product.

By condensation of the appropriate bromo-esters with ethyl sodioacetoacetate, followed by hydrolysis, we have prepared 8-*ketononoic acid* and 9-ketodecoic acid. Godchot and Coquil (*Compt. rend.*, 1931, **192**, 962) state that 8-ketononoic acid is obtained by the oxidation of α-methyl*cyclo*octanone with permanganate, but they do not describe the acid (they give m. p. 116—117° for the semicarbazone; we find m. p. 136°). Van Romburgh (*Akad. Amsterdam Versl.*, 1911, **20**, 195) obtained 9-ketodecoic acid by the oxidation of 2-keto-Δ^{10}-undecene and the melting point is given as 49°, which tallies with our observation.

At this stage further results on the degradation of carpaine came to hand (Barger, Robinson, and Work, this vol., p. 711). One of the products is a hydroxy-acid, $C_{13}H_{26}(OH)\cdot CO_2H$, which most likely has the constitution of 9-hydroxy-9-methyltridecoic acid ($CO_2H = 1$) and experiments on the synthesis of this acid are in progress. In the meantime we have prepared an isomeride, p-*phenylphenacyl* 8-*hydroxy*-8-*methyltridecoate*, $CH_3\cdot[CH_2]_4\cdot CMe(OH)\cdot[CH_2]_6\cdot CO\cdot O\cdot CH_2\cdot CO\cdot C_6H_4Ph$ (III), by interaction of ethyl 8-ketononoate with *n*-amylmagnesium bromide and eventual formation of the ester in the usual way. This substance does not appear to be identical with the specimen derived from carpaine. A synthesis of *ethyl 8-phenoxyoctoate* is described, but the yield is far from satisfactory. An attempt to improve the method by hydrolysing the product of condensation of 5-phenoxyvaleryl chloride and ethyl sodioacetosuccinate (cf. G. M. Robinson, J., 1930, 745) was unsuccessful and is not mentioned in the experimental section.

EXPERIMENTAL.

Ethyl Tetrahydrofurfurylmalonate.—Ethyl malonate (160 g.) and tetrahydrofurfuryl bromide (165 g.) were successively added to a solution of sodium ethoxide (23 g. of sodium) in absolute alcohol (300 c.c.), and the mixture refluxed (bath at 100—105°) for 16 hours. The alcohol was distilled, and the product isolated by means of ether. Unchanged bromide and ethyl malonate (total, 36 g.) were collected below 110°/1 mm., and *ethyl tetrahydrofurfurylmalonate* passed over at 123°/1 mm. as a colourless pleasant-smelling oil (Found: C, 59·5; H, 8·5. $C_{12}H_{20}O_5$ requires C, 59·0; H, 8·2%) (yield, 170 g. or 70%).

β-*Tetrahydrofurylpropionic Acid.*—A mixture of potassium hydroxide (80 g.), water (80 c.c.), alcohol (320 c.c.), and ethyl tetrahydrofurfurylmalonate (122 g.) was refluxed on the steam-bath for 6 hours. The alcohol was removed, the cooled residue diluted with water and washed with ether, and concentrated hydrochloric acid added with cooling in ice. The precipitated tetrahydrofurfurylmalonic acid was collected by means of ether as a pale yellow viscous oil, which would not crystallise even at – 20°. When the acid was heated at 140—160°, carbon dioxide was smoothly evolved, giving β-tetrahydrofurylpropionic acid as a pale brown oil (70 g.). On redistillation, the pure acid was obtained as a colourless, sharp-smelling, viscous oil, b. p. 119°/0·2

mm., $n_D^{15°}$ 1·4591 (Found: C, 58·3; H, 8·3. Calc. for $C_7H_{12}O_3$: C, 58·3; H, 8·3%). Kauffman and Adams (*loc. cit.*) record b. p. 135—137°/4 mm.

Ethyl β-Tetrahydrofurylpropionate.—The crude product from the above experiment was heated with alcohol (130 c.c.) and concentrated sulphuric acid (5 c.c.) on the steam-bath for 5 hours. Isolated in the customary manner, *ethyl β-tetrahydrofurylpropionate* was obtained as a colourless oil of pleasant pine-apple odour (58·5 g.), b. p. 105°/11 mm., $n_D^{15°}$ 1·4425 (Found: C, 62·5; H, 9·5. $C_9H_{16}O_3$ requires C, 62·8; H, 9·3%).

3-Tetrahydrofurylpropan-1-ol.—Ethyl tetrahydrofurylpropionate (64·5 g.), dissolved in absolute alcohol (625 c.c.), was added during 4 minutes to sodium (54·5 g.) in a flask heated in a bath at 145°. After 20 minutes, more alcohol (100 c.c.) was added, followed after 15 minutes by 50% alcohol (100 c.c.). The alcohol was removed by passing a current of steam for a short period, and the product isolated from the residue by means of ether. After drying of the extract and removal of the solvent, the residual oil was fractionated, 3-tetrahydrofurylpropan-1-ol being obtained as a colourless oil of faint odour, b. p. 111·5°/11 mm., $n_D^{15°}$ 1·4597 (yield, 36 g. or 75%). Bray and Adams (*J. Amer. Chem. Soc.*, 1927, **49**, 2105) give the b. p. 106—107°/2 mm. and Burdick and Adkins (*ibid.*, 1934, **56**, 441) record b. p. 106°/10 mm.

γ-Tetrahydrofurylpropyl chloride was prepared by the method of Gilman and Hewlett (*loc. cit.*). These authors give b. p. 75°/4 mm., but we have found b. p. 78°/11 mm., representing a considerable divergence (Found: C, 56·6; H, 8·7; Cl, 23·6. Calc. for $C_7H_{13}OCl$: C, 56·6; H, 8·8; Cl, 24·0%).

γ-Tetrahydrofurylpropyl Bromide.—A mixture of tetrahydrofurylpropyl alcohol (16·5 g.) and dry pyridine (1 c.c.) was added during ½ hour to a mixture of phosphorus tribromide (11·3 g.) and dry pyridine (1·5 c.c.) which was well stirred and maintained at 0°. After 4 hours, the product was distilled under diminished pressure. When the distillate was redistilled, the desired *bromide* was obtained as a colourless oil of characteristic odour, b. p. 100—101°/16 mm. On keeping, the liquid became cloudy, and it was therefore washed with water and taken up in ether, and the residue from the dried extract redistilled; b. p. unchanged (Found: Br, 41·1. $C_7H_{13}OBr$ requires Br, 41·5%) (yield, 16·5 g.). A copious precipitate of silver bromide was obtained when the bromide was gently heated with alcoholic silver nitrate.

Ethyl Bistetrahydrofurfurylmalonate.—Ethyl tetrahydrofurfurylmalonate (31 g.) and then tetrahydrofurfuryl bromide (21 g.) were added to a solution of sodium ethoxide (2·9 g. of sodium) in absolute alcohol (60 c.c.). The mixture was refluxed for 30 hours, the alcohol distilled, and the product isolated by means of ether. Fractionation gave unchanged bromide (3·5 g.) and ethyl tetrahydrofurfurylmalonate (17 g.), after which *ethyl bistetrahydrofurfurylmalonate* distilled as a colourless, very viscous oil (14 g.), b. p. 165°/0·5 mm. (Found: C, 62·1; H, 8·6. $C_{17}H_{28}O_6$ requires C, 62·2; H, 8·5%).

*ββ'-Bistetrahydrofuryl*iso*butyric Acid* (I).—The above ester was heated on the steam-bath with potassium hydroxide (15 g.), water (15 c.c.), and alcohol (60 c.c.) for 10 hours. After dilution with water and washing with ether, the alkaline solution was acidified with hydrochloric acid. The bistetrahydrofurfurylmalonic acid was extracted with ether, the extract dried, and the ether removed. The residual pale brown oil solidified incompletely at − 20°, and without further purification was heated to 120—140°: carbon dioxide was then smoothly evolved. On distillation *ββ'-bistetrahydrofuryl*iso*butyric acid* was obtained as a colourless viscous oil (6·3 g.), b. p. 173°/0·35 mm. (Found: C, 63·2; H, 8·8. $C_{12}H_{20}O_4$ requires C, 63·2; H, 8·8%).

Tetrahydrofurfuryl p-*Toluenesulphonate.*—A mixture of *p*-toluenesulphonyl chloride (96 g.), tetrahydrofurfuryl alcohol (51 g.), and dry ether was well stirred and cooled to − 5° to − 10° whilst finely powdered potassium hydroxide (56 g.) was added in small portions, the temperature being kept below 0°. Stirring was continued for ½ hour longer and the flask was then corked and kept, with frequent shaking, in the freezing mixture. After 2 hours, the mixture was poured into ice-water (800 c.c.), and after mechanical stirring for ½ hour the ethereal layer was separated, and the aqueous layer again extracted with ether (2 × 100 c.c.). The combined extracts were dried, and the ether removed, leaving a pale yellow oil (83—85 g.), which solidified, on cooling, in pale lemon crystals. A small portion, after several crystallisations from benzene and light petroleum, gave white needles, m. p. 38·7—39·1° (Found: S, 12·2. Calc. for $C_{12}H_{16}O_4S$: S, 12·5%).

Tetrahydrofurylacetonitrile.—A mixture of tetrahydrofurfuryl bromide (30 g.), potassium cyanide (20 g.), sodium iodide (1 g.), water (20 c.c.), and alcohol (35 c.c.) was refluxed for 35 hours. The product was isolated by means of ether and gave unchanged bromide (10 g.), b. p. 60—86°/17 mm., and then *tetrahydrofurylacetonitrile* (7 g.), b. p. 90—95°/15 mm., on distillation. In another experiment, using the same quantities as above, but no sodium iodide, the products were

4 g. of unchanged bromide and 8·1 g. of the nitrile. On redistillation the nitrile was obtained as a colourless oil of characteristic odour, b. p. 92·4°/13 mm., $n_D^{13°}$ 1·4476 (Found : N, 12·9. C_8H_9ON requires N, 12·6%).

Tetrahydrofurylacetic Acid.—A mixture of tetrahydrofurylacetonitrile (10 g.), alcohol (100 c.c.), potassium hydroxide (12 g.), and water (25 c.c.) was refluxed (10 hours) until ammonia was no longer evolved. The alcohol was distilled, the residue carefully acidified with concentrated hydrochloric acid, the mixture shaken several times with ether, the combined extracts dried, and the solvent removed. The residue, on distillation in a vacuum, gave *tetrahydrofurylacetic acid* as a colourless, extremely viscous oil (7·7 g.), b. p. 144—146°/16 mm., 140°/11 mm. (Found : C, 55·6; H, 7·8. $C_6H_{10}O_3$ requires C, 55·4; H, 7·7%). The substance did not solidify at − 20°.

12 : 12-*Dicarboxy*-13-*tetrahydrofuryltridecan*-1-*ol.*—A mixture of ethyl tetrahydrofurfurylmalonate (6·1 g.), 11-bromoundecanyl acetate (7·3 g.), and sodium ethoxide (0·58 g. of sodium) in absolute alcohol (20 c.c.) was refluxed for 5 hours. The product was isolated in the usual manner and heated to 170°/40 mm. in order to remove traces of volatile matter. Subsequently, a portion was heated to 330°/0·165 mm., but it did not distil. The substance (7 g.) was therefore heated on the steam-bath during 2½ hours with a mixture of water (4 c.c.), alcohol (16 c.c.), and potassium hydroxide (4 g.). The *acid* was isolated after removal of the alcohol, dried, triturated with benzene to free it from an insoluble gum, and crystallised several times from alcohol; ultimately, it crystallised from aqueous alcohol in small white needles, m. p. 108—109° (Found : C, 64·0; H, 9·5. $C_{19}H_{34}O_6$ requires C, 63·8; H, 9·5%).

Ethyl 2-Furoylacetate.—The following modification of Sandelin's method (*Ber.*, 1900, **33**, 492, 1176) gives this substance in a yield amounting to 93%.

Ethyl furoate was prepared by refluxing furoic acid ("Organic Syntheses," **6**, 44) with alcohol containing 10% of its volume of concentrated sulphuric acid for 4 hours. The high concentration of sulphuric acid (60% of the volume of alcohol used) recommended by Jackson and Hill (*J. Amer. Chem. Soc.*, 1890, **12**, 24) is unnecessary. The ester, isolated in the customary manner, crystallised in very pale brown prisms, m. p. 33—34°; Hill (*J. Amer. Chem. Soc.*, 1881, **3**, 38) gives the same m. p.

Ethyl furoate (24·8 g.) was heated at 80° and mechanically stirred, finely cut sodium (2 g.) added, and pure ethyl acetate (8·8 g., 9·8 c.c.) gradually introduced. When all the sodium had disappeared, the temperature of the bath was raised to 95°, and further sodium wire (2 g.) was introduced, followed by the dropwise addition of 8·8 g. of ethyl acetate. The mass soon became almost solid and dry benzene (50—60 c.c.) was then added. The addition of sodium wire (2 g.), followed by ethyl acetate (8·8 g.), was continued until a total of 12 g. of sodium and 57 g. of ethyl acetate had been used. After the fifth addition of sodium, it was necessary to add about 50 c.c. of dry benzene, and 1 hour after the final addition of sodium a further 20 c.c. of benzene were introduced in order to promote efficient stirring. After 12 hours' stirring, only a small amount of sodium remained and the mixture was cooled in ice, decomposed by the addition of ice-water, and poured into a well-stirred solution of hydrochloric acid (50 c.c.) in water (200 c.c.), a further 15 c.c. of the acid being added subsequently. After ½ hour's stirring, the benzene layer was separated, the aqueous layer extracted twice with ether, and the combined extracts dried. After removal of the solvents, the residue was fractionated: ethyl acetoacetate and ethyl furoate (total, 9 g.), b. p. up to 90°/20 mm., were first obtained and then the main fraction of ethyl furoylacetate, b. p. 110—115°/1 mm., was collected (32 g.). On redistillation, pure ethyl furoylacetate was obtained, b. p. 113—114°/1 mm., $n_D^{16°}$ 1·5055 (Found : C, 59·2; H, 5·6. Calc. for $C_9H_{10}O_4$: C, 59·3; H, 5·5%).

Ethyl 6-Chlorohexoate.—Thionyl chloride (7·5 g.) was added dropwise during 10 minutes to a mixture of ethyl 6-hydroxyhexoate (10 g.) and dry pyridine (5 c.c.), well stirred and maintained at 0°. After being stirred for 2 hours at 0° and 2 hours at room temperature, the liquid was decanted from the white crystals, which were then triturated several times with dry ether. The combined extracts were washed in turn with aqueous sodium carbonate, dilute hydrochloric acid, and water. It is essential to remove all the sulphur dioxide. When the residue from the dried extract was distilled, *ethyl 6-chlorohexoate* (9·1 g.) was obtained, b. p. 106—110°/15 mm., mostly 107—108°/15 mm. A redistilled specimen had b. p. 106°/14 mm., $n_D^{18°}$ 1·4398 (Found : Cl, 19·4. $C_8H_{15}O_2Cl$ requires Cl, 19·9%). Very similar results were obtained by using 40 g. of the hydroxy-ester.

Ethyl 6-Bromohexoate.—(A) A mixture of ethyl 6-hydroxyhexoate (20 g.) and pyridine (4 c.c.) was added during 45 minutes to phosphorus tribromide (12 g.) and pyridine (2 c.c.), well stirred and maintained at 0°. Stirring was continued for 2½ hours, and the mixture kept over-night.

After the addition of ice-water, the product was extracted with ether, the extract being washed with aqueous sodium carbonate and water. The residue from the dried extract, on distillation, gave a pleasant-smelling colourless oil (13 g.), b. p. 126—127°/20—21 mm. (Found: Br, 32·0. $C_8H_{15}O_2Br$ requires Br, 35·9%). In addition, there was obtained a residue (4—5 g.), b. p. 215—220°/1 mm.

(B) A more satisfactory method was the following: Ethyl 6-hydroxyhexoate (30 g.) was added to a cooled mixture of hydrobromic acid (250 c.c., *d* 1·5) and sulphuric acid (60 c.c.) and kept at room temperature for 2 hours with occasional shaking. After being heated on the steam-bath for 4 hours, the mixture was cooled, diluted with water and saturated with ammonium sulphate and the bromo-acid was collected by means of ether and esterified by refluxing with alcohol (50 c.c.) and sulphuric acid (2·5 c.c.) for 8 hours. The *ester* was isolated in the usual manner, there being obtained 31 g., b. p. 122—125°/12 mm. (Found: Br, 33·0%), and not more than 1 c.c. of residue.

The above result has been duplicated on several occasions; but from one experiment, on the same scale as above, there was obtained a liquid (31 g.), b. p. 132—134°/14 mm. When ethyl 6-hydroxyhexoate (14·5 g.) was allowed to react with a mixture of hydrobromic acid (110 c.c.) and sulphuric acid (20 c.c.) containing 0·2 c.c. of α-heptenylheptaldehyde, first at room temperature for 1 hour and then on the water-bath for 4 hours, a slow stream of oxygen being passed continuously through the liquid, the bromo-ester (13·0 g.) finally obtained had b. p. 134—145°/22 mm. In another experiment, the hydroxy-ester (40 g.) was treated with hydrobromic acid (320 c.c.) and sulphuric acid (60 c.c.) in the presence of α-heptenylheptaldehyde and oxygen, under precisely the same conditions as the above; the bromo-ester (36·5 g.) finally isolated had b. p. 127—130°/19 mm.

Ethyl 7-Bromoheptoate.—(A) To a mixture of phosphorus tribromide (2·9 g.) and dry pyridine (0·5 c.c.), well stirred and maintained at 0°, ethyl 7-hydroxyheptoate (5 g.) was added dropwise during 20 minutes. The mixture was subsequently stirred for 2 hours at 0° and for 3 hours at 15°. The product was isolated in the usual manner and refluxed with alcohol (10 c.c.) and sulphuric acid (0·5 c.c.) during 4 hours. The *ester* was obtained as a pleasant-smelling oil (4·8 g.), b. p. 135—139°/17 mm., mostly 135°/17 mm. (Found: C, 47·4; H, 7·3. $C_9H_{17}O_2Br$ requires C, 45·5; H, 7·2%. $C_9H_{18}O_3$ requires C, 62·2; H, 10·4%). Obviously the bromo-ester is contaminated with a little of the hydroxy-ester.

(B) Ethyl 7-hydroxyheptoate (25 g.) was allowed to react with a mixture of hydrobromic acid (200 c.c., *d* 1·7) and sulphuric acid (50 c.c.) during 1 hour at room temperature and 3 hours on the steam-bath. The crude bromo-acid was isolated as above and refluxed with alcohol (50 c.c.) and sulphuric acid (2·5 c.c.) during 7 hours. The bromo-ester had b. p. 129—136°/12 mm., mostly 132°/12 mm.; yield, 20 g.

Ethyl α-Acetylsuberate.—Ethyl acetoacetate (17·5 g.) and ethyl 6-bromohexoate (31 g.) were added in turn to a solution of sodium ethoxide (3·1 g. of sodium) in absolute alcohol (100 c.c.), and the mixture refluxed for 9 hours. The product was isolated in the known manner and on distillation gave *ethyl α-acetylsuberate* (18 g.), b. p. 148—165°/0·28 mm., mostly 154—158°/0·28 mm., and a residue of about 10 g.

When ethyl sodioacetoacetate (sodium, 2·1 g.; ethyl acetoacetate, 12 g.) and ethyl 6-chlorohexoate (16 g.) were allowed to react in alcohol in the presence of a little anhydrous sodium iodide during 14 hours at 110—120°, and the product isolated as usual, there was obtained a liquid, b. p. 140—160°/0·7 mm., mostly 156—160°/0·7 mm. Redistillation gave ethyl α-acetylsuberate, b. p. 158°/0·7 mm. (Found: C, 61·9; H, 9·0. $C_{14}H_{24}O_5$ requires C, 61·7; H, 8·8%). The crude ethyl α-acetylsuberate is always contaminated by a small amount of ethyl suberate.

8-*Ketononoic Acid.*—The crude ethyl α-acetylsuberate (8 g.) was shaken during 3 hours with aqueous (300 c.c.) potassium hydroxide (7·5 g.) at room temperature. The solution was extracted with ether, acidified with dilute hydrochloric acid, and saturated with ammonium sulphate, and the product extracted with ether. The ether was removed without drying, and the residue heated with 5% sulphuric acid (50—100 c.c.) for ½ hour. The keto-acid was taken up in ether, the extract dried, and the ether removed. The residues from several such experiments were united and purified as follows. The keto-acid is freely soluble in hot light petroleum, whereas suberic acid is insoluble. The crude acid was therefore warmed with light petroleum (b. p. 40—60°), the solvent decanted, and the process repeated until no more could be extracted. The residue from the combined extracts was the pure *keto-acid*, white needles, m. p. 40—41°; after one crystallisation, m. p. 40·5—42° (Found: C, 62·9; H, 9·1. $C_9H_{16}O_3$ requires C, 62·8; H, 9·3%). The 2 : 4-*dinitrophenylhydrazone* was readily obtained and formed small yellow needles from methyl alcohol, m. p. 88—89° (Found: N, 15·4. $C_{15}H_{20}O_6N_4$ requires N, 15·9%).

The *semicarbazone* formed short thick prisms, m. p. 136°, from methyl alcohol–light petroleum (Found : N, 18·1. $C_{10}H_{19}O_3N_3$ requires N, 18·3%).

Ethyl 8-Ketononoate.—8-Ketononoic acid (17·5 g.) was refluxed with alcohol (30 c.c.) containing sulphuric acid (1·5 c.c.) during 6 hours. The ester was isolated in the usual manner, b. p. 141—142°/11 mm. (Found : C, 65·9; H, 10·2. $C_{11}H_{20}O_3$ requires C, 66·0; H, 10·0%); yield, 18·3 g. The *semicarbazone* was readily obtained, and after recrystallisation from aqueous alcohol, was again crystallised from benzene and light petroleum; it formed silky needles, m. p. 108° (Found : N, 16·3. $C_{12}H_{23}O_3N_3$ requires N, 16·3%).

p-*Phenylphenacyl 8-Ketononoate*.—8-Ketononoic acid (0·34 g.) was suspended in water (5 c.c.) and not quite neutralised with *N*-sodium hydroxide; alcohol (10 c.c.) was then added, followed by *p*-phenylphenacyl bromide (0·55 g.) (Drake and Bronitsky, *J. Amer. Chem. Soc.*, 1930, **52**, 3715), and the mixture refluxed for 1 hour. When the product was cooled, an almost quantitative yield of white crystals was obtained, which after recrystallisation from ethyl alcohol formed colourless prisms, m. p. 93·5—95° (Found : C, 75·6; H, 7·3. $C_{23}H_{26}O_4$ requires C, 75·4; H, 7·1%).

9-Ketodecoic Acid.—To a solution of sodium (2·4 g.) in absolute alcohol (100 c.c.), ethyl acetoacetate (13·7 g.) and ethyl 7-bromoheptoate (25 g.) were added in turn, and the mixture heated at 100—110° for 5½ hours. The product was isolated in the usual manner. Distillation gave 18 g. of a liquid, b. p. 145—160°/0·27 mm., mostly 151—152°/0·27 mm., and 5 g. of a residual dark oil. The crude ethyl α-acetylazelate (18 g.) was shaken during 3·5 hours at room temperature with potassium hydroxide (12·5 g.) in water (500 c.c.). After washing with ether, the alkaline solution was acidified with dilute hydrochloric acid, and the mixture heated on the water-bath for ½ hour. The liquid was cooled, saturated with ammonium sulphate, and extracted with ether, the extract dried, and the solvent removed entirely (crude product, 10·7 g. or 91·5%). The keto-acid was purified in the same manner as 8-ketononoic acid. 9-Ketodecoic acid crystallised from light petroleum in white needles, m. p. 47·5—48·5° (Found : C, 64·5; H, 9·7. Calc. for $C_{10}H_{18}O_3$: C, 64·6; H, 9·7%). The *semicarbazone* was readily prepared, and after crystallisation from ethyl acetate formed hard white crystals, m. p. 127° (Found : N, 15·2; loss at 80° in a vacuum, 11·7. $C_{11}H_{21}O_3N_3,2H_2O$ requires N, 15·1; H_2O, 12·9%). Curiously enough, the semicarbazone crystallised from aqueous methyl alcohol in glistening plates, m. p. 115—116°, which were anhydrous (Found : no loss at 100° in a vacuum; N, 17·1. $C_{11}H_{21}O_3N_3$ requires N, 17·3%).

Ethyl 9-Ketodecoate.—The keto-acid was refluxed with alcohol (20 c.c.) and sulphuric acid (1·5 c.c.) during 7 hours, and the ester (8·4 g.) isolated as usual, b. p. 154—156°/13 mm.; Ruzicka and Stoll (*Helv. Chim. Acta*, 1927, **10**, 691) record b. p. 151—153°/11 mm. The semicarbazone formed glistening plates from alcohol, m. p. 97—98° (Found : N, 15·4. Calc. for $C_{13}H_{25}O_3N_3$: N, 15·5%). Ruzicka and Stoll (*loc. cit.*) record m. p. 102—103°.

p-*Phenylphenacyl 9-ketodecoate*, prepared from 9-ketodecoate (0·2 g.) and *p*-phenylphenacyl bromide (0·2 g.) precisely as for the similar compound above, and twice crystallised from methyl alcohol, was obtained in almost colourless prisms, m. p. 68—70° (Found : C, 76·0; H, 7·4. $C_{24}H_{28}O_4$ requires C, 75·8; H, 7·4%).

p-*Phenylphenacyl 8-Hydroxy-8-methyltridecoate* (III).—A Grignard reagent prepared from fresh magnesium turnings (0·7 g.), *n*-amyl bromide (4·85 g.), and dry ether (30 c.c.) with the help of a trace of iodine was slowly added to a well-stirred solution of ethyl 8-ketononoate (5·0 g.) in ether (100 c.c.). The addition caused the formation of a white precipitate and stirring was continued for 6 hours at room temperature and next day the mixture was heated at 70—80° for 3 hours, with stirring. The product was cooled in ice and mixed with water and ammonium chloride; the ethereal layer was separated, and the aqueous portion extracted several times with small amounts of ether. The residue from the dried extracts, after being exposed in a vacuum, weighed 6·7 g. This was shaken with semicarbazide hydrochloride (3 g.), sodium acetate (5 g.), alcohol (20 c.c.), and water (15 c.c.) for 6 hours. The semicarbazone (1 g.) which separated was collected, and the oil extracted from the filtrate. The ether was removed, and the residue allowed to remain with a solution of potassium hydroxide (2 g.) in water (5 c.c.) and alcohol (10 c.c.). After 3½ hours, the product was diluted with water, extracted several times with small amounts of ether, and the aqueous portion then acidified with dilute hydrochloric acid at 0°. The white precipitate was collected in ether, the residue from the dried extract being an oil (3 g.) which would not solidify. It was therefore added to an ethereal solution (40 c.c.) of diazomethane (from 10 g. of nitrosomethylurea) and after 3 hours the excess of diazomethane was decomposed with a little acetic acid, and after the addition of alkali, the ethereal layer was separated; the aqueous portion was again extracted, and the combined extract dried. After removal of

the ether, the residue was distilled: fraction (1) had b. p. 90—122°/0·03 mm., and fraction (2) (0·8 g.) had b. p. 123—130°/0·03 mm., mostly 126—130°/0·03 mm. Analysis of fraction (2) (Found: C, 69·0; H, 11·3. $C_{11}H_{20}O_3$ requires C, 66·0; H, 10·0%. $C_{15}H_{30}O_3$ requires C, 69·8; H, 11·6%) showed it to be a mixture of the desired hydroxy-ester and unchanged keto-ester. The oil was saturated to permanganate, it being necessary to warm gently before the colour was discharged. The ester was hydrolysed during 3 hours with potassium hydroxide (0·2 g.) dissolved in 70% alcohol (7 c.c.); the product was diluted with water and extracted with ether. The alkaline solution was acidified, and the precipitated acid extracted with ether, the residue (0·58 g.) from the dried extract being a viscous oil which did not solidify at low temperatures. It was therefore treated with *p*-phenylphenacyl bromide (0·45 g.) precisely as described above for another such derivative. A yellow oil was thus obtained which did not solidify on cooling. It was therefore treated with ether, washed with water, a little alkali, and finally water, and the ethereal solution was then dried. The resultant pale yellow oil gave a sticky solid when cooled in ice; but after being rubbed with a drop of alcohol, and standing for 5 days, it had formed a mass of white needles. These were collected, washed with a drop of cold alcohol, dried on a porous tile, and recrystallised from light petroleum (m. p. 62—69° at this stage) and finally from alcohol. As crystallisation was delayed (3 days), the concentrated solution was triturated with a little light petroleum, whereby white crystals were obtained, m. p. 68—71° (Found: C, 77·1; H, 8·7. $C_{28}H_{38}O_4$ requires C, 76·8; H, 8·7%). This is obviously the p-*phenylphenacyl* ester of 8-*hydroxy*-8-*methyltridecoic acid*.

A similar experiment with *n*-butylmagnesium bromide and ethyl 9-ketodecoate was unsuccessful, because at the final stage *p*-phenylphenacyl 9-ketodecoate was isolated, m. p. 66—68° alone or mixed with an authentic specimen. Doubtless the desired hydroxy-acid was present, but instead of purifying it by the preparation of the derivative we unfortunately purified and isolated the unchanged starting material.

Ethyl γ-Phenoxypropylacetoacetate.—Ethyl acetoacetate (70 g.) and γ-phenoxypropyl bromide (108 g.) were added to a solution of sodium ethoxide (11·6 g. of sodium) in absolute alcohol (200 c.c.), and the mixture refluxed on the steam-bath for 30 hours. The alcohol was distilled and, after the addition of water, the *product* was isolated by means of ether as a colourless liquid of faint fruity odour, b. p. 164°/1 mm., $n_D^{18°}$ 1·5018 (Found: C, 68·4; H, 7·6. $C_{15}H_{20}O_4$ requires C, 68·2; H, 7·5%) (yield, 93·5 g. or 71%).

As a by-product, there were obtained 15—20 g. of a pale yellow, viscous oil, b. p. 240—250°/0·35 mm. (Found: C, 72·1; H, 7·6. $C_{24}H_{30}O_5$ requires C, 72·3; H, 7·5%). On redistillation this substance had b. p. 220°/0·06 mm., and solidified on cooling. After recrystallisation from light petroleum, it formed fine silky needles, m. p. 61—62° (Found: C, 72·4; H, 7·7%). The substance is therefore *ethyl di(phenoxypropyl)acetoacetate*.

Products of Hydrolysis of Methyl 4-Keto-5-acetyl-5-carbethoxy-8-phenoxyoctoate.—Ethyl phenoxypropylacetoacetate (98·5 g.) was added to pulverised sodium (8·65 g.) under dry benzene (200 c.c.) and when all the sodium had passed into a clear golden solution carbomethoxypropionyl chloride (62 g.) was added, and the mixture refluxed for 16 hours. The product was cooled and diluted with water, and the benzene layer separated. The aqueous phase was again extracted twice with ether, the combined extracts dried, and the solvent removed. The crude product was then shaken during 24 hours with potassium hydroxide (88 g.) dissolved in water (2640 c.c.). The alkaline solution was extracted with ether in order to remove unchanged ester. The alkaline solution was acidified with hydrochloric acid, the liberated acid being collected by means of ether. Examination of the two ethereal extracts showed that only one-fourth of the total ester had been hydrolysed. The residual ester was therefore shaken during 60 hours with 2 l. of 5% potassium hydroxide solution, which process reduced the amount of unchanged ester by 50%. This residue was shaken with 5% potassium hydroxide solution (800 c.c.) and an equal volume of acetone for 2 days. The still considerable amount of unchanged ester was shaken during 1 week with 5% potassium hydroxide solution (800 c.c.); only a small portion then remained undissolved. The various acid fractions were united and refluxed for 5 hours with 5% sulphuric acid (600 c.c.), the product being isolated by means of ether. It was then boiled for 12 hours with aqueous potash (70 g. in 3500 c.c.). The alkaline solution (A) was extracted with ether, the extract dried, and the solvent removed. Distillation of the residue gave *methyl δ-phenoxybutyl ketone* (22·5 g.) as a pale lemon oil of pleasant odour, b. p. 136—137°/1 mm., 102—103°/0·02 mm., $n_D^{13°}$ 1·5143 (Found: C, 75·2; H, 8·7. $C_{12}H_{16}O_2$ requires C, 75·0; H, 8·3%). The 2 : 4-*dinitrophenylhydrazone*, readily prepared and recrystallised from alcohol, formed small yellow needles, m. p. 97—98° (Found: N, 15·2. $C_{18}H_{20}O_5N_4$ requires N, 15·1%).

The alkaline solution (A) was acidified and extracted with ether, the extract dried, and the

ether removed. The residue (about 25 g.) was reduced by the method of Clemmensen, following precisely the directions of Le Sueur and Withers (J., 1915, **107**, 736). The reduction mixture was finally extracted with benzene, from which, in turn, the organic acids were extracted with sodium hydroxide. Acidification gave a dark brown oil, which solidified incompletely in ice. The whole was therefore refluxed with alcohol (40 c.c.) and sulphuric acid (1 c.c.) for 5 hours. The product was rendered alkaline with potassium carbonate, and extracted with ether. The residue from the dried extract was fractionally distilled, two fractions being obtained : (1) *ethyl 5-phenoxyvalerate*, b. p. 115—117°/0·42 mm. (Found : C, 70·8; H, 8·1. $C_{13}H_{18}O_3$ requires C, 70·3; H, 8·1%) (yield, 8·5 g.). A portion of this ester was hydrolysed by means of 10% aqueous potash at room temperature to 5-phenoxyvaleric acid, m. p. 64·5—65·5°, not lowered by admixture with an authentic sample. The fraction (2) was ethyl 8-phenoxyoctoate, b. p. 135—140°/0·42 mm. (3 g.). This was hydrolysed by means of aqueous alkali to 8-*phenoxyoctoic acid*, which crystallised from light petroleum (b. p. 40—60°) in glistening white plates, m. p. 68—70°, unchanged after three recrystallisations (Found : C, 70·9; H, 8·5. $C_{14}H_{20}O_3$ requires C, 71·2; H, 8·5%).

5-*Phenoxyvaleric Acid and its Chloride.*—Ethyl γ-phenoxypropylacetoacetate (69 g.) was heated on the steam-bath during 5 hours with potassium hydroxide (70 g.), water (50 c.c.), and alcohol (60 c.c.). After 12 hours at room temperature, water was added, and the mixture shaken with ether in order to remove alkali-insoluble matter (3 g. of methyl δ-phenoxybutyl ketone). The alkaline solution was acidified with hydrochloric acid and the precipitated 5-phenoxyvaleric acid, which solidified after cooling in ice, was collected, washed with water, and dried (44 g.). A small portion, recrystallised from light petroleum, formed white needles, m. p. 62·5—63·5°.

5-Phenoxyvaleric acid (47·5 g.) was heated at about 40° for 3 hours with purified thionyl chloride (40 g.). The excess of thionyl chloride was removed in a vacuum; the residue gave 5-phenoxyvaleryl chloride (34 g.), b. p. 142—144°/8 mm. After standing for 2 days in a sealed vessel, it solidified to a mass of white needles, m. p. 44·5—45·0°. The acid chloride was characterised through the *anilide*, which formed glistening white plates from light petroleum, m. p. 84·5—85·5° (Found : N, 5·2. $C_{17}H_{19}O_2N$ requires N, 5·2%).

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144. *The Structure of the Glutaconic Acids and Esters. Part IX. α-Methyl- and α-Ethyl-glutaconic Acids.*

By J. S. Fitzgerald and G. A. R. Kon.

It has been shown by Kon and Watson (J., 1932, 2434) that the well-known α-benzylglutaconic acid is the *trans*-form with the double bond in the βγ-position (I, R = CH_2Ph), and a new isomeride, the *cis*-Δ^{α}-acid (II, R = CH_2Ph) was also described.

(I.) $CO_2H{\cdot}CHR{\cdot}CH{:}CH{\cdot}CO_2H$ $\qquad$ $CO_2H{\cdot}CR{:}CH{\cdot}CH_2{\cdot}CO_2H$ (II.)

The corresponding α-methyl- and α-ethyl-acids have now been examined.

The stable forms of the acids have been prepared by a slight modification of the method of Thole and Thorpe (J., 1911, **99**, 2208); the preparation of the ethyl acid was very tedious owing to the ready fission of the parent carboxyglutaconic ester with the production of butyric acid. Since Kon and Watson (*loc. cit.*) had found it impossible to esterify the α-benzyl acid without isomerisation, even by the silver salt method, an attempt was made to prepare the methyl esters of these acids with the aid of diazomethane in the cold. The ester of the α-methyl acid prepared in this way was homogeneous and the products obtained from it on ozonisation (oxalic acid, derived from the methyl glyoxylate first formed, and methyl α-formylpropionate) showed that the parent acid had the formula (I, R = Me). The ester of the α-ethyl acid was similar, although the neutral oxidation product could not be identified with certainty.

These stable acids are therefore the Δ^{β}-compounds of the structure (I), and doubtless have the *trans*-configuration, since they are not the primary products obtained by the hydration of the anhydrides formed from them.

The latter method is the only one available for the preparation of the *cis*-forms and presents considerable experimental difficulties. For instance, it is difficult to obtain the hydroxy-anhydride of the α-methyl acid free from the corresponding chloro-anhydride, the presence of which is prejudicial because it liberates hydrogen chloride on hydration; and we were unable to obtain the hydroxy-anhydride of the α-ethyl acid in a pure condition. Moreover, the conditions employed by Thole and Thorpe and also by Feist (*Annalen*, 1909, **370**, 41) for the hydration of these anhydrides involve the use of alkali and are therefore unsuitable. For this reason we adopted the method of Malachowski (*Ber.*, 1929, **62**, 1323), who used cold water. The hydrolysis under these conditions is slow and some hydroxy-anhydride remains unchanged at the end of two months, whilst the interconversion of the two forms of the acid under these conditions proceeds at a comparable rate, so that the *trans*-acid is isolated at the end of the experiment. However, if the acid formed is isolated at the end of a few hours, the *cis*-form is obtained and in this way the pure *cis*-α-methyl *acid* was prepared. It melts some 7° higher than the "labile" acid of Thole and Thorpe (= *cis*-acid of Feist); the latter acid is doubtless the eutectic of the two forms similar to that formed from the α-benzyl acids. The new acid has the Δ^{α}-structure (II, R = Me), as shown by the ozonisation of the ester prepared by means of diazomethane: no oxalic acid was produced, and methyl pyruvate was identified in the neutral portion of the products.

Owing to our failure to obtain the pure hydroxy-anhydride of the α-ethyl acid, the pure *cis*-form of this acid was not obtained; the acid of m. p. 108° (Thole and Thorpe, *loc. cit.*) was isolated, but ozonisation of the ester proved that it was not homogeneous, since oxalic acid was detected in the mixture of oxidation products.

EXPERIMENTAL.

trans-*α-Methyl-Δ^{β}-propene-αγ-dicarboxylic Acid* (I, R = Me).—The stable form of α-methylglutaconic acid was prepared by Linstead and Millidge's modification of Thole and Thorpe's method (J., 1936, 478), but it was found possible to hydrolyse ethyl α-methyl-αγ-dicarboxyglutaconate in one stage by keeping it for 10 days with an excess of 30% aqueous potassium hydroxide and enough alcohol to give a homogeneous solution. The yield of crude acid obtained was somewhat less than 50% and a 65% yield was obtained by hydrolysing ethyl α-methyl-γ-carboxyglutaconate under the same conditions. In either case the acid obtained was evidently contaminated with some acid ester, as the amount diminished considerably on recrystallisation; the pure acid melted at 145°. The methyl ester was prepared by adding the acid slowly to a freshly prepared solution of diazomethane in dry ether, the reagent being present in excess. After some hours the solution was evaporated, and the residue distilled; the ester had b. p. 92—93°/1·5 mm., $d_{4^{\circ}}^{20\cdot5^{\circ}}$ 1·1055, $n_{D}^{20\cdot5^{\circ}}$ 1·4578, $[R_L]_D$ 42·44.

Ozonisation. The ester, dissolved in 5 vols. of ethyl acetate, was cooled in ice and treated with ozonised oxygen until no more was absorbed. The solvent was removed under reduced pressure below 40°, and the residue decomposed by shaking with cold water for some hours and finally warmed with water under reflux for 15 minutes. The products were taken up in ether, and the extract shaken with aqueous sodium bicarbonate, which removed oxalic acid; this was identified in the usual way. The ethereal extract was dried and evaporated and was shown to contain methyl α-formylpropionate by preparing 1-phenyl-4-methylpyrazolone, m. p. and mixed m. p. 148—149°, from it with phenylhydrazine.

cis-*α-Methyl-Δ^{α}-propene-αγ-dicarboxylic Acid* (II, R = Me).—The *trans*-acid was heated with acetyl chloride (2 mols.) in a sealed tube for 5—6 hours at 110°: in some experiments a crystalline solid, m. p. 70—76°, separated in small amount. The liquid was evaporated to dryness, the residue taken up in ether, and the solution extracted with aqueous sodium bicarbonate until the latter remained alkaline; the dark red extract was acidified with dilute hydrochloric acid and extracted with ether. The extract was still highly coloured, but a colourless preparation was obtained by distilling the hydroxy-anhydride under reduced pressure in a sabre flask; the yield did not exceed 40%. Hydration under Thole and Thorpe's conditions gave an acid, m. p. 110—118°, consisting mainly of the *cis*-acid. To prepare the pure *acid*, the hydroxy-anhydride was finely powdered and left covered with water for several hours; the water was

then evaporated without heating in a vacuum desiccator at 2 mm.; a solid was then obtained, m. p. 123—125°, which was crystallised from chloroform. The m. p., now 125—126°, was depressed by the *trans*-acid (Found: C, 49·7; H, 5·7. $C_6H_8O_4$ requires C, 50·0; H, 5·6%). The methyl ester was prepared with diazomethane and had b. p. 82—85°/2 mm., $d_{4°}^{18·5°}$ 1·1041, $n_D^{18·5°}$ 1·4546, $[R_L]_D$ 42·24.

Ozonisation. This was carried out as described on p. 726. No oxalic acid was obtained; the neutral portion gave the usual colour reactions of pyruvates and methyl pyruvate was identified as the 2 : 4-dinitrophenylhydrazone, m. p. 180°; it also gave a violet colour with ferric chloride.

trans-*α-Ethyl-Δ^β-propene-αγ-dicarboxylic Acid* (I, R = Et).—Both the tricarboxylic and the tetracarboxylic ester in this case gave an acid contaminated with various amounts of butyric acid, although both acid and alkaline hydrolytic agents were tried; the method described on p. 726 was on the whole the best. The acid after several crystallisations had m. p. 131—132° (Thole and Thorpe give m. p. 133—134°). The methyl ester was prepared with diazomethane and had b. p. 95—98°/5 mm., $d_{4°}^{19·0°}$ 1·0762, $n_D^{19·0°}$ 1·4574, $[R_L]_D$ 47·10.

Ozonisation. This was carried out as before; oxalic acid was isolated in large quantity and identified. The neutral product reacted with phenylhydrazine, but the resulting pyrazolone would not crystallise (1-phenyl-4-ethylpyrazolone is described as melting at 78°).

cis-*α-Ethylglutaconic Acid.*—All attempts to obtain a pure hydroxy-anhydride from the *trans*-acid were unsuccessful; the material prepared as described on p. 726 was semi-solid and crude *cis*-acid could be prepared from it by rubbing with benzene; after recrystallisation from chloroform this melted at 108—109°. The methyl ester prepared from it had b. p. 90—96°/5 mm., $d_{4°}^{19·0°}$ 1·0728, $n_D^{19·0°}$ 1·4558, $[R_L]_D$ 47·12. The products obtained on ozonisation are referred to on p. 726.

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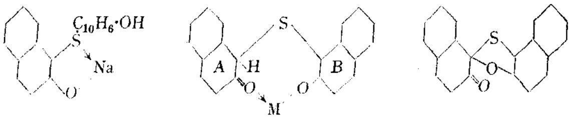
145. *Covalent Alkaline Derivatives of Di-2-hydroxy-1-naphthyl Sulphide and of Di-2-hydroxy-1-naphthylmethane.*

By WILFRID J. EVANS and SAMUEL SMILES.

ATTEMPTS to isolate the disodium salt of di-2-hydroxy-1-naphthyl sulphide from aqueous alkaline media yielded an insoluble and stable *monosodium* salt (compare Lesser and Gad, *Ber.*, 1925, **58**, 2557). Further examination of this substance showed that, isolated from aqueous media, it has the composition $C_{20}H_{13}O_2SNa,4H_2O$; it melts at 255°, is insoluble in water, moderately soluble in warm benzene or chloroform, and is strikingly characterised by its high solubility in ether. These properties show that the substance contains the metal in the covalent state (Sidgwick and Plant, J., 1925, **127**, 209; Sidgwick and Brewer, *ibid.*, p. 2379). In assigning a structure to the compound the alternatives (I) and (II) must be considered, but the former is rejected since di-2-hydroxy-1-naphthylmethane (II; S replaced by CH_2) yields a *monosodium* derivative of analogous composition and closely similar properties. The structure (II) is therefore adopted; it is further supported by the facts: (1) The monomethyl ether, obtained from this monosodium derivative by methylation or by synthesis from 2-naphthol and 1-bromothiol-2-methoxynaphthalene (Warren and Smiles, J., 1931, 918), is only slightly soluble in warm dilute aqueous sodium hydroxide and no sodium salt has been obtained from it; also in other reactions which will be described later it gives evidence of the structure indicated. (2) The dehydro-derivative (III) (Warren and Smiles, J., 1930, 956) is quantitatively formed from the monosodium derivative by oxidation (J., 1914, **105**, 1750). (3) Simple aromatic di-*o*-hydroxy-sulphides such as di-4-hydroxy-*m*-tolyl sulphide, which do not yield monomolecular dehydro-derivatives (compare III), do not under similar conditions give sodium derivatives of this character. The influence of substitution in the aromatic nuclei on the behaviour of sulphides of this type will be discussed on a future occasion. Facts similar to those mentioned in (1), (2) and (3) have been observed with derivatives of the analogous methane series.

Experiments have been extended to the derivatives of di-2-hydroxy-1-naphthyl sulphide and di-2-hydroxy-1-naphthylmethane containing other metals; the former yielded



(I.) (II.) (III.)

covalent *monoalkali* derivatives (II; M as metal) with lithium ($4H_2O$ and $2H_2O$), sodium ($4H_2O$), potassium ($2H_2O$), and rubidium ($2H_2O$ and anyhdrous), and the latter gave the lithium ($4H_2O$), sodium ($4H_2O$) and potassium ($2H_2O$) derivatives. With the exception of the rubidium derivative mentioned, none of these could be dehydrated completely by heating at 100° or by other means.

The apparently anomalous composition of the tetrahydrates of the lithium derivatives requires further comment. It is suggested that the inclusion of the two additional water molecules by these substances is required for the easy attainment of the crystalline state; this view is supported by experiments made with the lithium derivative of the sulphide, which showed a reluctance to crystallise as a dihydrate. For example, the crystalline tetrahydrate of this substance is readily formed in presence of excess of water, but when a warm dilute solution of the tetrahydrate in benzene is rapidly cooled, a gelatinous material of indefinite composition is deposited; the crystalline dihydrate was obtained only by slow cooling of this solution. All the metallic derivatives mentioned are very soluble in ether; some evidence has been obtained of the presence of etherates in these solutions and of the formation of additive products with esters, but a closer examination of these has not yet been made.

One of the more interesting features of this series of covalent derivatives is the relative stability of the 8-membered co-ordinate ring which they contain; moreover, a certain flexibility of this ring seems evident from the formation of both the rubidium derivative of the sulphide and the lithium derivative of dihydroxynaphthylmethane. In seeking an explanation of this circumstance it may be noted that the stereochemical relation of the sulphur atom (or CH_2) to each naphthalene nucleus in (II) is different and it is suggested that this condition, by permitting a non-coplanar arrangement, facilitates chelation and enhances the stability of the ring which is then formed. Attemps to obtain, under the conditions described, similar covalent derivatives from 2 : 2′-dihydroxy-1 : 1′-dinaphthyl and from di-2-hydroxy-1-naphthyl disulphide have been unsuccessful; the behaviour of the disulphide seems the more interesting, since it is known (Stevenson and Smiles, J., 1930, 1745) that this substance yields a dehydro-derivative (III; S replaced by -S·S-) on oxidation in alkaline solution and is therefore present in such media in the hydroxy-ketonic state required for the formation of the chelate ring.

In structures (II) of the type now encountered it is clear that a resonant condition of the system containing the metallic atom implies the facile attainment of the extreme phases, $A{=}O{\rightarrow}Na - O{-}B$ and $A{-}O - Na{\leftarrow}O{=}B$, which differ from each other not only in the sequence of the various linkages but also in the alternate situation of the 1-hydrogen atom at the nucleus A or B respectively. Resonance of the system $=O\rightarrow M - O-$ would thus appear also to require resonance of hydrogen between the two α-positions. There are several evident reasons for regarding this condition as impossible; perhaps the chief of these is that a change in the stereochemical arrangement of members of the ring would be involved; it is therefore concluded that co-ordinate linkage of the alkali metals in these substances is established without resonance of the systems formed. These considerations are of interest in view of the work of Sidgwick (*Ann. Reports*, 1933, 112; 1934, 40), who has shown that there are fundamental reasons for concluding that the co-ordination of hydrogen requires resonance of the system in which it occurs and thus differs from the mechanism of co-ordination by metals. No definite evidence concerning

the structure of the parent hydroxy-compounds can at present be adduced, but it is worth notice that in the case of 2-hydroxy-1-naphthyl sulphide all the alkali derivatives examined are characterised by their high solubility in moist ether, whereas the parent hydroxy-compound is only slightly soluble in this medium.

EXPERIMENTAL.

Unless otherwise stated, all the metallic derivatives described were dried before examination in a current of nitrogen at 25—35°; they were readily soluble in cold ether and moderately soluble in hot benzene, toluene or chloroform. In hot solvents such as those mentioned, partial dehydration sometimes occurred. The m. p.'s recorded must be regarded as approximate and as depending to a certain extent on the rate of heating; in nearly all cases water was lost before the m. p. was reached.

Derivatives of Di-2-hydroxy-1-naphthyl Sulphide.—Sodium derivative. A suspension of the finely powdered sulphide (1 mol.) in 5% sodium hydroxide solution (2 mols.) was stirred and warmed until all had dissolved. The desired *product* separated in pale yellow plates from the cooled solution. It was dried for analysis in a current of air at 25°. It lost some water at about 100° and finally melted at 255°; attempts completely to dehydrate the substance by heating in a vacuum (115°) over phosphoric oxide were unsuccessful (Found: C, 58·8; H, 5·3; Na, 5·5. $C_{20}H_{13}O_2SNa,4H_2O$ requires C, 58·3; H, 5·1; Na, 5·5%). It was also analysed by determining the sulphide liberated after treatment with dilute sulphuric acid (Found: sulphide, 76·5. $C_{20}H_{13}I_2O_2SNa,4H_2O$ requires sulphide, 77·1%). The monomethyl ether of di-2-hydroxy-1-naphthyl sulphide separated when methyl alcohol containing this sodium derivative and methyl iodide was boiled (1 hour). It had m. p. 155° and was identical with the product previously (J., 1931, 918) obtained by synthesis (Found: C, 75·5; H, 4·9. Calc.: C, 75·9; H, 4·8%). The dimethyl ether was obtained by boiling (3 hours) a solution of the sulphide (1 mol.), sodium methoxide (3 mols.), and methyl iodide in methyl alcohol. It formed colourless prisms, m. p. 184°, not depressed by the yellow product (m. p. 185°) obtained (J., 1913, **103**, 345) from 2-methoxynaphthalene and sulphur chloride (Found: C, 76·7; H, 4·9. Calc.: C, 76·3; H, 5·2%).

The *lithium* derivative separated in the crystalline state when a solution of the sulphide (1 mol.) in hot aqueous lithium hydroxide (5%; 2 mols.) was cooled (Found: C, 60·8; H, 5·4. $C_{20}H_{13}O_2SLi,4H_2O$ requires C, 60·6; H, 5·3%). The monomethyl ether of the sulphide was obtained from this substance by reaction with methyl iodide in hot methyl alcohol. When a dilute solution of this tetrahydrate in hot benzene was slowly cooled, the *dihydrate* was obtained in prisms (Found: C, 66·9; H, 4·7. $C_{20}H_{13}O_2SLi,2H_2O$ requires C, 66·7; H, 4·7%).

The *potassium* derivative was obtained in the crystalline state when a hot solution of the sulphide (1 mol.) in aqueous potassium hydroxide (4·5%; 2 mols.) was slowly cooled. After being dried as usual, it had m. p. 230° (Found: C, 61·1; H, 4·4; K, 9·7. $C_{20}H_{13}O_2SK,2H_2O$ requires C, 61·2; H, 4·3; K, 9·9%). Dehydration was incomplete after heating (120°) in nitrogen (2 hours).

The *rubidium* derivative was obtained by shaking the finely powdered sulphide (1 mol.), aqueous rubidium hydroxide (2 mols.; 6%) and rubidium chloride with a little ether. The crystalline material, which separated when the ethereal solution was kept, was purified from warm benzene; the product, after being dried in nitrogen at 80°, was the *dihydrate*, which had m. p. 210° (Found: C, 55·1; H, 3·5; Rb, 19·4. $C_{20}H_{13}O_2SRb,2H_2O$ requires C, 54·7; H, 3·9; Rb, 19·5%). Further dehydration was effected by heating in a current of nitrogen at 120°. The *anhydrous* material then obtained had m. p. 212° (Found: C, 60·4; H, 3·5. $C_{20}H_{13}O_2SRb$ requires C, 59·6; H, 3·2%).

Di-3-bromo-2-hydroxy-1-naphthyl Sulphide.—The *sodium* derivative was obtained by stirring the sulphide (1 mol.) with aqueous sodium hydroxide (3 mols.; 4%) and rapidly filtering the mixture. When the clear solution was kept, the product separated in pale yellow needles, m. p. 300° after being dried as usual (Found: C, 45·3; H, 2·8. $C_{20}H_{11}O_2Br_2SNa,2H_2O$ requires C, 44·9; H, 2·8%).

Di-2-hydroxy-1-naphthylmethane.—The *sodium* derivative was obtained as leaflets by cooling a solution of the dihydroxynaphthylmethane (1 mol.) in warm aqueous sodium hydroxide (2 mols.; 5%). This product, after some loss of water at 100°, had m. p. 255° (Found: C, 63·3; H, 5·4; Na, 5·8. $C_{21}H_{15}O_2Na,4H_2O$ requires C, 63·9; H, 5·8; Na, 5·8%). In hot methyl alcohol it was converted by methyl iodide or methyl sulphate into the *monomethyl* ether of di-2-hydroxy-1-naphthylmethane, which formed needles, m. p. 142°, sparingly soluble in cold alcohol and only slightly soluble in warm 2*N*-sodium hydroxide (Found: OMe, 9·9. $C_{22}H_{18}O_2$ requires

OMe, 9·9%). With acetic anhydride (100°, 30 mins.), it furnished an *acetyl* derivative, which formed needles from acetic acid, m. p. 131—133° (Found : C, 80·5; H, 5·7; OMe, 8·5. $C_{24}H_{20}O_3$ requires C, 80·9; H, 5·6; OMe, 8·7%). This acetyl derivative is also formed by prolonged interaction of hot acetic anhydride and di-2-methoxy-1-naphthylmethane, m. p. 148—149° (Kohn and Ostersetzer, *Monatsh.*, 1918, **39**, 302).

The *lithium* derivative separated in the crystalline state when a hot solution of the dihydroxynaphthylmethane (1 mol.) in aqueous lithium hydroxide (2 mols.; 3%) was cooled (Found: C, 66·5; H, 6·0; Li, 1·8. $C_{21}H_{15}O_2Li,4H_2O$ requires C, 66·7; H, 6·1; Li, 1·8%). The substance, like the lithium derivative of the sulphide, had no melting point, apparently passing into the electrovalent state at high temperatures. It yielded the monomethyl ether by reaction with methyl iodide in methyl alcohol, and when the cold solution in moist ether was mixed with benzene it was recovered (Found : C, 66·3; H, 6·2%).

The *potassium* derivative separated in needles when a hot solution of di-2-hydroxy-1-naphthylmethane (1 mol.) in aqueous potassium hydroxide (2 mols.; 4·5%) was cooled (Found : C, 66·9; H, 4·9; K, 10·0. $C_{21}H_{15}O_2K,2H_2O$ requires C, 67·4; H, 5·1; K, 10·4%). It lost some water at 100° and then melted at 245°. Di-2-hydroxynaphthylmethane is also soluble in a more dilute, hot solution of potassium hydroxide (1·4 mols.; 1·5%); when this solution was cooled, a different and more complex *potassium* derivative separated. This had m. p. 170° and was very soluble in moist ether (Found : C, 73·8; H, 4·9; K, 5·5. $C_{21}H_{15}O_2K,C_{21}H_{16}O_2,2H_2O$ requires C, 74·8; H, 5·2; K, 5·8%).

A further examination of this group of substances is being made.

We wish to thank Mr. C. S. McClement for the data concerning the sodium derivative of di-2-hydroxy-1-naphthyl sulphide.

KING'S COLLEGE, LONDON. [*Received, January 15th*, 1937.]

146. *The Constituents of Senega Root. Part I. α-Spinasterol.*

By JAMES C. E. SIMPSON.

THE literature being notably devoid of information regarding the constituents of senega root other than senegin, an investigation of this problem has been commenced, attention being first directed to the lipoidal fraction of an alcoholic concentrate of the root. This concentrate, after removal of senegin, consisted principally of ether-insoluble material which, although sparingly soluble in water, dissolved in aqueous sodium hydroxide. Extraction of the alkaline solution with ether yielded a comparatively odourless, fatty oil moderately rich in non-saponifiable matter, which consisted of a partly crystalline, viscous mass having a highly characteristic and not unpleasant odour. Benzoylation of this material furnished a mixture, from which a product of constant m. p. 200° was isolated. By hydrolysis of this benzoate a sterol, m. p. 169—170°, was obtained, which was converted into its acetate, m. p. 184—185°, and *p*-nitrobenzoate, m. p. 213·5—215°. These three compounds are identical with α-spinasterol, its acetate, and *p*-nitrobenzoate, for samples of which the author is greatly undebted to Dr. Heyl.

α-Spinasterol, already examined by Hart and Heyl (*J. Biol. Chem.*, 1932, **95**, 311) and Larsen and Heyl (*J. Amer. Chem. Soc.*, 1934, **56**, 2663), has now been further characterised. It was recovered unchanged in 80% yield after treatment with maleic anhydride under the conditions employed for the combination of the latter with ergosterol (Windaus and Luttringhaus, *Ber.*, 1931, **64**, 850), and therefore conjugation of its two ethenoid linkages is excluded, despite the apparent nuclear similarity of the two sterols. This conclusion is supported by the ultra-violet absorption spectrum of α-spinasterol, which, though resembling that of ergosterol qualitatively, has an extinction coefficient which is only 0·5% of that of the latter substance. The possibility that this slight absorption is due to the presence in senega root of a trace of ergosterol (or other similarly constituted sterol) is being investigated. The sterol gives a transient but definite faint pink coloration with antimony trichloride in chloroform; this behaviour, however, is also observed with the sterol recovered from the maleic anhydride treatment.

In the hope of obtaining information as to the position of one or both of the unsaturated

centres, a preliminary study was made of the behaviour towards chromic anhydride and perbenzoic acid of α-spinasterol and its acetate. The free sterol was oxidised smoothly by the former reagent at room temperature to the corresponding ketone, *α-spinastadienone*, m. p. 176° (*oxime*, m. p. 253°). Similar oxidation of the acetate on the other hand gave a mixture of neutral products, from which two crystalline *substances* were isolated. The less soluble substance, $C_{30}H_{46}O_3$, m. p. 211—213°, on hydrolysis readily yielded the corresponding *alcohol*, $C_{28}H_{44}O_2$, m. p. 152°. The second product of this oxidation had m. p. 170°; the analytical data indicated the formula $C_{30}H_{46}O_4$ (or $C_{30}H_{48}O_4$). Unlike the acetate $C_{30}H_{46}O_3$, however, this substance underwent decomposition on hydrolysis, and no homogeneous product was isolated. The structures of these products are under investigation; the course of the oxidation bears a formal resemblance to that of cholesteryl acetate ($C_{29}H_{48}O_2 \longrightarrow C_{29}H_{46}O_3 + C_{29}H_{48}O_4$; Windaus and Kirchner, *Ber.*, 1920, **53**, 614) and α-ergostenyl acetate ($C_{30}H_{50}O_2 \longrightarrow C_{30}H_{48}O_3 + C_{30}H_{48}O_4$; Heilbron, Simpson, and Wilkinson, J., 1932, 1699).

Titrations of α-spinasterol with perbenzoic acid (Larsen and Heyl, *loc. cit.*) show that the oxygen equivalent of two double bonds is ultimately taken up. It has now been found that treatment of the sterol with this reagent in approximately equimolecular proportion furnishes *α-spinasterol oxide*, m. p. 165°, in good yield. The same product is obtained by similar treatment of α-spinasteryl acetate, followed by saponification of the resultant *α-spinasteryl acetate oxide*, m. p. 159°.

In many of its properties α-spinasterol stands in marked contrast to the sterols which have hitherto been investigated in detail. Attempts, for example, to hydrate α-spinasterol oxide under a variety of conditions (compare Morrison and Simpson, J., 1932, 1710; Coffey, Heilbron, and Spring, *J.*, 1936, 738; Fernholz, *Annalen*, 1934, **508**, 215) have proved unsuccessful, whereas the oxides of cholesterol, sitosterol, stigmasterol, and α-dihydrofucosterol are all more or less readily converted into the corresponding triols. A further difference between the sterols cited and α-spinasterol is the fact that the latter forms neither a di- nor a tetra-bromide. This was observed by Larsen and Heyl (*loc. cit.*) and has been confirmed in this laboratory (see experimental). Thirdly, the melting points of the esters of α-spinasterol are considerably higher than those of the other sterols, and the characteristic high lævorotation of sterols containing a 5 : 6-double bond is not exhibited by α-spinasterol (see Table I). Lastly, the absorption spectrum of α-spinastadienone shows only two extremely faint bands at 2520 A. and 2440 A., whereas ketones derived from $\Delta^{5:6}$-unsaturated sterols, *e.g.*, cholestenone (Menschick, Page, and Bossert, *Annalen*, 1932, **495**, 225) and α-fucostenone (Coffey, Heilbron, and Spring, *loc. cit.*), exhibit the intense absorption at about 2450 A. characteristic of αβ-unsaturated ketones.

The possibility that these striking anomalies might be ascribable to the presence of a pentacyclic (triterpenoid) skeleton in the molecule of α-spinasterol is difficult to reconcile

TABLE I.

	Sterol.		Acetate.		Propionate.	Benzoate.
	M.p.	$[\alpha]_D$.	M.p.	$[\alpha]_D$.	M.p.	M.p.
Cholesterol	148°	−37·8°	114°	−43° [1]	98°	150°
Sitosterol	137	−26·7 [2]	127	−36 [3]	108 [3]	145 [3]
Stigmasterol	170	−45 [4]	141	−50·3 [5]	122 [4]	160 [4]
Fucosterol	124	−38·4 [6]	119	−43·8 [6]	105 [6]	120 [6]
α-Spinasterol	170	− 1·8 [7]	185	− 4·7 [7]	153 [7]	201 [7]

[1] Bergman, *J. Biol. Chem.*, 1934, **107**, 527. [2] Burian, *Monatsh.*, 1897, **18**, 551. [3] Anderson, Shriner, and Burr, *J. Amer. Chem. Soc.*, 1926, **48**, 2987. [4] Windaus and Hauth, *Ber.*, 1906, **39**, 4378. [5] Anderson and Shriner, *J. Amer. Chem. Soc.*, 1926, **48**, 2976. [6] Heilbron, Phipers, and Wright, J., 1934, 1572. [7] Hart and Heyl, *loc. cit.*

with the properties of the compound. Thus its isolation (together with the isomeric β-spinasterol) *via* the digitonide has been described by Heyl and Larsen (*J. Amer. Pharm. Assoc.*, 1933, **22**, 510). Furthermore the physical constants of the spinastenols and of spinastanol (Larsen and Heyl, *loc. cit.*) are typically those of hydrogenated sterols. Finally, the analytical data are in markedly better agreement with the requirements of a tetra-

cyclic, rather than a pentacyclic, nucleus. There are therefore reasonable grounds for regarding α-spinasterol as a true sterol. The anomalies noted are thus presumably due to a distribution of double bonds in α-spinasterol not hitherto encountered in sterols of known constitution, and lead to the provisional suggestion that this sterol differs from other sterols in that it does not contain the 5 : 6-double bond characteristic of the latter.

EXPERIMENTAL.

(Melting points uncorrected; specific rotations in chloroform.)

Isolation of α-Spinasteryl Benzoate.—Senega root (1 part) was digested thrice with boiling alcohol (5 parts), and the extract filtered hot. The crude senegin which separated on cooling was removed, and the filtrate concentrated as completely as possible under reduced pressure. The resultant soft gum was dissolved in sodium hydroxide (3 l. of 4% solution per 2 kg. of gum) by continued shaking at room temperature, and the solution after slight dilution with water was extracted with ether for 3 days in a continuous-extraction apparatus. The extract was filtered from a small amount of glycosidic material, and the residual fatty oil (1 part) was refluxed for 3 hours with potassium hydroxide in 90% alcohol (10 parts of 10%). Most of the alcohol was removed, and the residue was then largely diluted with water and extracted with ether. Evaporation of the washed and dried extract gave a semi-crystalline mass (7—8% of the fatty oil), which was dissolved in its own weight of pyridine and treated with the same amount of benzoyl chloride. After standing over-night, the product was decomposed with ice and sulphuric acid and worked up by ether-extraction, etc. Digestion of the dry residue with a little acetone gave a crystalline product, which was recrystallised once from acetone and then repeatedly from ethyl acetate, large plates of the benzoate, m. p. 199·5—200·5°, being finally obtained (2·9 g. from 630 g. of the fatty oil) (Found: C, 83·9; H, 10·1. Calc. for $C_{35}H_{50}O_2$: C, 83·6; H, 10·0%).

α-Spinasterol.—The above benzoate was refluxed for 2 hours with 5% alcoholic potassium hydroxide; the sterol, which separated from alcohol in small plates, had m. p. 169—170° both alone and when mixed with authentic α-spinasterol, and $[\alpha]_D^{17°}$ − 3·7° (c = 1·35, l = 1) (Hart and Heyl, *loc. cit.*, give $[\alpha]_D^{25°}$ − 1·8°).

α-Spinasteryl Acetate.—This was obtained quantitatively from the sterol with acetic anhydride (alone or with pyridine) and crystallised from ethyl acetate in large plates, m. p. 184·5—185·5°. A mixture with authentic α-spinasteryl acetate of identical m. p. gave no depression. It had $[\alpha]_D^{17°}$ − 4·0° (c = 2·32, l = 1), the value of Hart and Heyl (*loc. cit.*) being $[\alpha]_D^{23°}$ − 4·7° (Found: C, 81·6; H, 10·8. Calc. for $C_{30}H_{48}O_2$: C, 81·75; H, 11·0%).

α-Spinasteryl p-*Nitrobenzoate.*—This was prepared in the usual manner and separated from ethyl acetate–alcohol in fine silky needles which melted at 213·5—215° and gave no depression when mixed with authentic α-spinasteryl *p*-nitrobenzoate of the same m. p. It had $[\alpha]_D^{17°}$ + 5·8° (c = 2·33, l = 1). Hart and Heyl (*loc. cit.*) give $[\alpha]_D^{23°}$ + 4·5°.

α-Spinastadienone.—The sterol (160 mg.) was dissolved in warm 95% acetic acid (60 c.c.) and cooled to 25—30°. The suspension was treated during 10 minutes with chromic anhydride (40 mg.) in glacial acetic acid (10 c.c.) and water (0·3 c.c.) and left at 20° overnight. The clear solution was then concentrated under reduced pressure, and the residue treated with dilute sulphuric acid and extracted with ether. The neutral fraction (140 mg.) on recrystallisation from acetic acid, alcohol, or acetone yielded small plates, m. p. 176—176·5°, which had $[\alpha]_D^{17°}$ + 19·5° (c = 0·77, l = 1) (Found: C, 84·6; H, 11·3. $C_{28}H_{44}O$ requires C, 84·8; H, 11·2%).

The *oxime*, prepared in the usual manner, separated from chloroform–methyl alcohol in small plates, m. p. 253—255° (decomp.) (Found: N, 3·9. $C_{28}H_{45}ON$ requires N, 3·4%).

α-Spinasteryl Acetate Oxide.—A solution of α-spinasteryl acetate (460 mg.) in chloroform (10 c.c.) was treated at 0° during 3—4 minutes with a chloroform solution of perbenzoic acid (6·2 c.c.; 1 double bond requires 5·4 c.c.) and left at 5° for 17 hours. The chloroform was removed at room temperature, and the crystalline residue taken up in ether, which was washed with sodium carbonate solution and water and dried. Recrystallisation of the product from acetone gave the pure *oxide* (340 mg.) in parallelograms, m. p. 158·5—159°, $[\alpha]_D^{17°}$ 1·4° (c = 2·67, l = 1) (Found: C, 79·3; H, 10·5. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%).

α-Spinasterol Oxide.—The acetate oxide was refluxed for 2½ hours with 5% methyl-alcoholic potassium hydroxide. The product separated from 90% acetone in prisms, m. p. 164—165° alone or mixed with the *oxide*, m. p. 165°, prepared directly from α-spinasterol and perbenzoic acid (Found: C, 81·4; H, 10·9. $C_{28}H_{46}O_2$ requires C, 81·1; H, 11·2%).

Oxidation of α-Spinasteryl Acetate.—To a solution of the acetate (500 mg.) in glacial acetic acid (150 c.c.), chromic anhydride (270 mg.; 3·2 atoms of oxygen) in water (0·5 c.c.) and glacial

acetic acid (10 c.c.) was added in portions during ½ hour at 25°. The solution was left at 20° for 22 hours, methyl alcohol then added, and the solvent removed under reduced pressure. The residue was treated with dilute sulphuric acid, extracted with ether, and separated into acid and neutral fractions with 2% sodium hydroxide solution. The neutral fraction (460 mg.) in alcohol deposited 160 mg. of sparingly soluble, crystalline material, which on repeated crystallisation from absolute alcohol or acetone formed heavy prismatic rods, m. p. 211—213·5° (Found: C, 79·1; H, 10·2. $C_{30}H_{46}O_3$ requires C, 79·2; H, 10·2. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%). An attempt to form an oxime under the ordinary conditions gave a product, m. p. 191—193°, which contained less than 0·5% of nitrogen.

The above acetate was refluxed for 2 hours with 4% alcoholic potassium hydroxide; the solution was then concentrated to half its original volume, and the product precipitated with water and extracted with ether. The residue from the washed, dried, and evaporated extract crystallised from dilute alcohol or acetone in prismatic needles, m. p. 151—152° (Found: C, 81·35; H, 11·0. $C_{28}H_{44}O_2$ requires C, 81·5; H, 10·75. $C_{28}H_{46}O_2$ requires C, 81·1; H, 11·2%).

The alcoholic filtrate from the 160 mg. described above was evaporated, and the residue dissolved in methyl alcohol. The crystalline product which separated was repeatedly crystallised from methanol, small crops of m. p. above 171° being discarded, until the bulk of the material was obtained in soft flattened needles of constant m. p. 170—171°, unchanged by recrystallisation from aqueous acetone (Found: C, 76·6; H, 10·1. $C_{30}H_{46}O_4$ requires C, 76·5; H, 9·9. $C_{30}H_{48}O_4$ requires C, 76·2; H, 10·2%).

Action of Bromine on α-Spinasteryl Acetate.—An ice-cold suspension of the acetate (100 mg.) in glacial acetic acid (4 c.c.) and dry ether (8 c.c.) was treated with bromine (40 mg., added in portions during 10 minutes); hydrogen bromide was freely evolved. The now clear solution was diluted with water and extracted with ether, and the extract washed with sodium carbonate solution and water, dried, and evaporated. An alcoholic solution of the semi-crystalline residue yielded unchanged α-spinasteryl acetate (m. p. and mixed m. p. 183°; 50 mg.), the filtrate from which contained only an unstable and highly soluble oil.

The author wishes to thank Dr. R. A. Morton for his kindness in determining the spectrographic data for α-spinasterol and α-spinastadienone.

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147. *The Ether-soluble Constituents of Sarsaparilla Root. Part I.*

By James C. E. Simpson and Norman E. Williams.

The nature of the constituents of sarsaparilla root has become, on biogenetic grounds, a matter of considerable interest in view of the recent advances that have been made in the chemistry of its two principal sapogenins, sarsasapogenin and smilagenin (van der Haar, *Rec. trav. chim.*, 1929, **48**, 726; Jacobs and Simpson, *J. Biol. Chem.*, 1934, **105**, 501; *J. Amer. Chem. Soc.*, 1934, **56**, 1424; Simpson and Jacobs, *J. Biol. Chem.*, 1935, **109**, 573; **110**, 565; Askew, Farmer, and Kon, J., 1936, 1399). The literature is seemingly devoid of information on this subject, with the notable exception of a paper by Power and Salway (J., 1914, **105**, 201), who carried out a qualitative investigation of the root and claimed to have isolated as the principal lipoids sitosterol, stigmasterol, cetyl alcohol, and a mixture of acids. The identification of these products was however based on somewhat meagre evidence; their characterisation of the sterols, in particular, must now be regarded as inadequate in the light of recent developments in phytosterol chemistry, for no comparison with authentic derivatives appears to have been made. Thus the evidence for the presence of stigmasterol (isolation of a tetrabromoacetate) does not exclude the possible presence of brassicasterol, which forms a tetrabromoacetate of similar melting point (Windaus and Welsch, *Ber.*, 1909, **42**, 612). The presence of sitosterol (also incompletely characterised) has likewise been observed by van der Haar (*loc. cit.*).

In the hope of placing these earlier findings on an unequivocal basis we have commenced a systematic examination of the ether-soluble (*i.e.*, non-saponaceous) constituents of the root. The results, now described, of a preliminary semi-quantitative survey of certain

fractions of the material show in some respects noteworthy differences from those of Power and Salway (*loc. cit.*).

The ether-soluble material was first separated into several main fractions by means of the scheme shown in the experimental part. The bulk of the sterols was found in fraction D, from which they were readily isolated by saponification and benzoylation of the non-saponifiable material, crystallisation of the mixed benzoates yielding a product of constant m. p. 144—145°. The materials obtained by hydrolysis and subsequent acetylation of this product had physical constants approximating to those of the sitosterol and sitosteryl acetate of Power and Salway, but consisted of a complex mixture of sterols, of which a partial separation was effected as follows.

Bromination of the mixed acetates by the method of Windaus and Hauth (*Ber.*, 1906, **39**, 4378) furnished a considerable proportion of a sparingly soluble bromoacetate, m. p. 210°; this was debrominated, hydrolysed, and converted into the corresponding *anisate*, m. p. 174°, and p-*nitrobenzoate*, m. p. 203°. Through the kindness of Professor Windaus, to whom we are greatly indebted for the supply of a sample of stigmasterol, we have been able to prepare authentic derivatives of the latter for comparison with those of the sarsaparilla sterol. The identity of this sterol with stigmasterol has by this means been conclusively established.

The filtrate from the stigmasteryl tetrabromoacetate was debrominated and saponified, and the physical constants of the product were found to resemble those of an ordinary sitosterol mixture. In view of the difficulty of separating such a mixture (or the acetates) into chemical individuals by fractional crystallisation from alcohol (Anderson and co-workers, *J. Amer. Chem. Soc.*, 1926, **48**, 2976, 2987; Bonstedt, *Z. physiol. Chem.*, 1928, **176**, 269) systematic fractional crystallisation from *cyclo*hexane of the 3 : 5-dinitrobenzoates of the mixed sterols was adopted and two apparently pure compounds were thus isolated. The less soluble *ester*, m. p. 215—217°, gave analytical figures indicating the formula $C_{35}H_{56}O_6N_2$, corresponding to the formula $C_{29}H_{50}O$ for the free sterol, which had m. p. 143—144° (acetate, m. p. 127—128°). Since none of the isomeric sitosterols or their acetates has physical constants in agreement with those of this sterol or its acetate, we propose for it the name ε-sitosterol. It appears to be present only in minute amount.

The second apparently pure 3 : 5-dinitrobenzoate had m. p. 207—209°; the corresponding sterol (which, allowing for the necessarily incomplete separation, probably constitutes about 50% of the total sitosterol mixture) melted at 135° and yielded an acetate, m. p. 126—127°, and benzoate, m. p. 146°. The close agreement between the melting points and specific rotations of these derivatives (see experimental) and those of the β-sitosterol of wheat-germ oil (Ichiba, *Inst. Phys. Chem. Res., Tokyo*, 1935, **28**, 112) indicates that the two substances are identical.

Fraction A (see scheme) consisted largely of fats and waxes, which liquefied at room temperature, together with a mixture of paraffins. The latter were isolated by fractional crystallisation and appeared, from the results of analysis and molecular-weight determinations, to have the mean formula $C_{18}H_{38} \pm CH_2$. In view of the illuminating work of Chibnall, Piper, Pollard, Smith, and Williams (*Biochem. J.*, 1931, **25**, 2095) on the composition of apple-wax, the possibility of resolution into individual substances by fractional crystallisation of the sarsaparilla paraffins would appear remote. The latter substances appear to be of lower molecular weight than the apple paraffins, and it is by no means certain that they are straight-chain compounds, since they melt at appreciably higher temperatures than normal paraffins of similar molecular weight (compare Piper, Chibnall, Hopkins, Pollard, Smith, and Williams, *ibid.*, p. 2072).

After the paraffins had been removed as completely as possible from fraction A, the filtrates were saponified. The non-saponifiable material (fraction B) was a complex mixture, of which little separation has as yet been effected. By means of phthalic anhydride there were isolated (i) a paraffin fraction, m. p. 55—57°; (ii) a small quantity of sterols, apparently a mixture similar to that already described; and (iii) after benzoylation of the original material, an unidentified compound which we are provisionally designating as *substance X*. This compound gave analytical data suggestive of the formula $C_{25}H_{24}O_7$. It is apparently the dibenzoate of a dihydric phenol $C_{11}H_{14}O_3(OH)_2$, this partial formula being supported

by the results of quantitative saponification. Attempts to isolate the product of hydrolysis —other than benzoic acid—proved unsuccessful. Small amounts of this substance, which has m. p. 124—125°, were also isolated from fractions C and F. Filixic acid, which occurs in male ferns, forms a benzoate of similar melting point (Daccomo, *Ber.*, 1888, **21**, 2962), but in view of the highly controversial literature dealing with this acid (see, for instance, Boehm, *Annalen*, 1901, **318**, 253) the identity of the two substances can only be regarded as speculative.

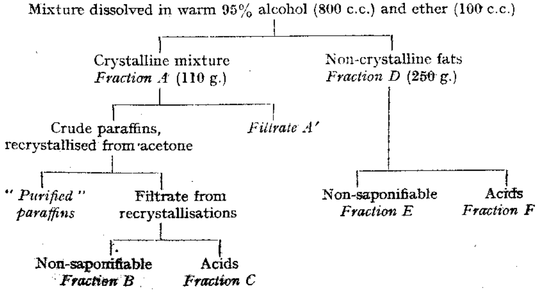
It is somewhat remarkable that the paraffins already mentioned have apparently not been encountered by previous workers, particularly as they appear to be highly characteristic components of the root, a fact which we have demonstrated by working with a different sample of root (commercial Mexican). The ether-soluble material was treated in the same way as that obtained from the Honduras root, the hydrocarbons being isolated as before from fraction A. The melting point (70°) was, however, considerably higher than that of the Honduras paraffins, and the analysis indicated contamination with non-paraffinoid substances. For the removal of the latter we employed the method of selective adsorption on aluminium oxide (Winterstein and Stein, *Z. physiol. Chem.*, 1933, **220**, 247, by this method quantitatively resolved a mixture of 99% of hentriacontane and 1% of pentadecyl ketone) and thus readily resolved the mixture of m. p. 70° into three distinct fractions. The main fraction (90% of the whole) was completely non-adsorbable and consisted of a paraffin or mixture of paraffins of m. p. 61—62° and mean formula $C_{23}H_{48}$. The second fraction (9%) was moderately strongly adsorbed; after purification by re-adsorption it had m. p. 82°. Analysis indicated the probable formula $C_{20}H_{42}O$, and its inertness towards acylating reagents and semicarbazide suggests that it is a tertiary alcohol. Owing to the small amount available it has been impossible further to characterise this substance. The third fraction, which was tenaciously held by the alumina, was a substance of probable formula $C_{29}H_{58}O_3$ and melting point 102—104°. It was present only in minute quantity (1% of the original mixture) and has not so far been characterised.

The investigation is being continued.

EXPERIMENTAL.

(Melting points uncorrected; specific rotations in chloroform.)

Honduras sarsaparilla root was exhausted by percolation with 95% alcohol, and the resultant solution concentrated under reduced pressure to a thick syrup. This was digested with a large volume of ether, and the ethereal solution decanted from the insoluble saponaceous gum, which was redigested with fresh ether. The united ethereal solutions were freed from solvent, and 1 kg. of the residue (corresponding to 43·5 kg. of root) was dissolved in ether (2 l.). After standing for 2—3 days at 10°, the solution was filtered from a little insoluble material and shaken first with 2*N*-sodium carbonate (5—6 times) and then with 6% aqueous sodium hydroxide until this was practically colourless. The neutral solution was then thoroughly washed with water, dried, and evaporated; the residual fatty material (360 g.) was resolved into fractions according to the scheme :



Fraction A.—This was dissolved in ethyl acetate to remove adhering oily material and three successive crops of crystalline material were removed (leaving the filtrate A′) which on fractionation from acetone by the triangle scheme yielded several fractions consisting of a mixture of paraffins (17 g.), m. p. 57—59° (Found for the main fraction : C, 85·2, 85·3; H, 15·3, 15·2; *M*, 211, 260, 236. $C_{18}H_{38}$ requires C, 84·9; H, 15·1%; *M*, 254).

The acetone filtrates from the most soluble fractions were united and evaporated, yielding an oil (44 g.), which was found to contain sterols. A portion was benzoylated in pyridine, and the product dissolved in acetone, in which the sterol benzoates (see below, fraction D) were sparingly soluble. No crystalline product could be obtained, indicating that the sterols were mostly, if not entirely, present in the form of waxes. The remainder of the oil (40 g.) was therefore refluxed for 2½ hours with alcoholic potassium hydroxide (500 c.c. of 6%), most of the solvent was then removed, and the residue largely diluted with water. Extraction with ether, followed by washing, drying, and evaporation of the extract, furnished a dark resinous material (fraction B, 17·5 g.).

Fraction B.—Separation of this mixture was attempted by the method of Chibnall *et al.* (*loc. cit.*); it was accordingly heated for 19 hours with phthalic anhydride (20 g.) at 120 ± 5°. The product was shaken with hot water, and the insoluble residue dissolved in ether. Only a negligible amount of material was extracted by shaking with warm 4% sodium carbonate solution, indicating the absence of primary aliphatic alcohols. The ethereal solution was then shaken with water, which removed the sparingly soluble sodium salts of the acid phthalates of a mixture of sterols. The latter were liberated by saponification and converted into the benzoates; the product appeared to be identical (m. p., mixed m. p., solubility) with the mixture of sterol benzoates, m. p. 143—144°, described under fraction D.

The residue (9·75 g.) from the dried and evaporated neutral ethereal solution was easily soluble in alcohol and was assumed from analogy with the experiments of Chibnall *et al.* (*loc. cit.*) to consist mainly of the sodium salts of the acid phthalates of secondary alcohols. It was therefore saponified under reflux for 18½ hours with 20% alcoholic potash (100 c.c.); after working up by the usual method a brown semi-crystalline product was obtained, which was esterified with benzoyl chloride in pyridine. The benzoylated material was isolated by the usual method (10·7 g.) and crystallised from acetone. The less soluble fractions consisted of a mixture of paraffins, m. p. 55—57° (Found : C, 85·4; H, 14·7; *M*, 314. $C_{23}H_{48}$ requires C, 85·1; H, 14·9%; *M*, 324). (In previous experiments direct crystallisation of fraction B, the phthalic anhydride treatment being omitted, yielded a paraffin mixture of m. p. 49—50°. Found : C, 85·2, 85·4; H, 15·2, 15·3%; *M*, 200, 263.)

The filtrate from the paraffins was evaporated, and the residue (6·9 g.) digested with warm ligroin; the crystalline material which separated was repeatedly crystallised from acetone–ligroin, ether–ligroin, and finally benzene, from which *substance X* separated in needles, m. p. 124·5—125° (Found : C, 69·0; H, 5·6. $C_{25}H_{24}O_7$ requires C, 68·8; H, 5·5%). The substance was recovered unchanged after refluxing with *N*/10-potassium hydroxide, but was saponified completely by refluxing for 8 hours with 5% alcoholic potassium hydroxide; with methyl-red as indicator, 69·7 mg. required 34·2 mg. of potassium hydroxide [$C_{11}H_{14}O_3(O{\cdot}CO{\cdot}C_6H_5)_2$ requires 35·8 mg. for 4 equivs.]. The saponified solution after titration was again made alkaline, distilled in steam, extracted with ether, and acidified. The benzoic acid was extracted with ether and purified by sublimation [yield, 36·5 mg. Calc. for $C_{11}H_{14}O_3(O{\cdot}CO{\cdot}C_6H_5)_2$, 39 mg.]. It was identified by m. p. and mixed m. p.; a mixture with the original substance melted at 80°.

The first ligroin filtrate from substance X yielded a small amount of the mixture of sterol benzoates, m. p. 143°.

Fraction C.—After acidification of the alkaline solution the acids were removed by threefold extraction with ether. The aqueous solution which remained was then re-extracted with ether for 3 days in a continuous-extraction apparatus. Evaporation of the dried extract left an oily residue, which gave positive colour reactions for glycerol; it was treated with benzoyl chloride in pyridine, but the only product isolated was a further quantity of substance X, m. p. 122—123° (from ether–ligroin) (Found : C, 68·5; H, 5·5%).

Filtrate A′.—This (43 g.) was saponified, and the non-saponifiable fraction benzoylated in the usual manner; a small quantity of the mixture of sterol benzoates was obtained as the sole crystalline product.

Fraction D.—After removal of solvent this was refluxed for 5½ hours with potassium hydroxide in 80% alcohol (2 l. of 12%). The non-saponifiable material (fraction E, 90 g.) was isolated by the usual method and benzoylated in pyridine. The product was treated with acetone (100 c.c.) and the crude crystalline material which separated was recrystallised from acetone

(which removed considerable amounts of easily soluble, crystalline substances) until it had m. p. 143—144° (4·8 g.).

Isolation of stigmasterol. The mixture of sterol benzoates was combined with the product obtained by similar treatment of a further kg. of starting material, and the whole (10·7 g.) was refluxed with alcoholic potash (5%). The free sterols (8·1 g., m. p. 135° from alcohol) were refluxed with acetic anhydride and the mixture of acetates (m. p. 128°) in ether (125 c.c.) was brominated by the method of Windaus and Hauth (*loc. cit.*). The product (2·25 g.) which separated on standing (m. p. 210—211°; crystallised from chloroform–alcohol) was refluxed for 1 hour with zinc dust (3 g.) and glacial acetic acid (55 c.c.). The product obtained by precipitation with water was recrystallised from alcohol and separated in glistening laminæ, m. p. 140—141° either alone or on admixture with authentic stigmasteryl acetate.

Saponification of the above acetate with alcoholic potash gave the free sterol, which formed plates from alcohol, m. p. 170°, $[\alpha]_D^{17^\circ}$ − 45·8° (c = 1·26, l = 1), and gave no depression in m. p. when mixed with authentic stigmasterol of m. p. 171° and $[\alpha]_D^{17^\circ}$ − 46·2° (c = 1·36, l = 1).

Stigmasteryl p-*nitrobenzoate.* This was prepared by heating the sterol (0·1 g.) with *p*-nitrobenzoyl chloride (0·2 g.) in pyridine (3 c.c.) on the water-bath for 3 hours; it separated from ligroin in silky needles which melted at 203° to a liquid of characteristic bluish-green fluorescence, and had $[\alpha]_D^{17^\circ}$ − 13·4° (c = 1·835, l = 1). The ester gave no depression in m. p. when mixed with a sample prepared from authentic stigmasterol, m. p. 203°, $[\alpha]_D^{17^\circ}$ − 13·3° (c = 0·58, l = 1) (Found: C, 76·9; H, 8·8; N, 2·7. $C_{36}H_{51}O_4N$ requires C, 77·1; H, 9·15; N, 2·5%).

Stigmasteryl anisate. This was prepared in a similar manner to the *p*-nitrobenzoate and separated from chloroform–methyl alcohol in plates, m. p. 173·5—174·5° to a fluorescent liquid; $[\alpha]_D^{17^\circ}$ − 14·3° (c = 1·212, l = 1). Authentic stigmasteryl anisate had the same m. p. and $[\alpha]_D^{17^\circ}$ − 15·1° (c = 1·017, l = 1), and a mixture of the two samples gave no depression in m. p. (Found: C, 81·7; H, 9·8. $C_{37}H_{54}O_3$ requires C, 81·3; H, 10·0%).

Fractionation of sitosterol mixture. The filtrate from the stigmasteryl tetrabromoacetate was debrominated by means of sodium amalgam and finally with zinc dust and acetic acid. Saponification of the halogen-free product was effected in the usual manner, 3·84 g. of a crystalline mixture of sterols being obtained; this was thoroughly dried and esterified with 3 : 5-dinitrobenzoyl chloride in pyridine (35 c.c.), the product being decomposed with ice and sulphuric acid and extracted with ether. The solution was washed with 1% aqueous sodium hydroxide and water, dried, and evaporated. A solution of the residue in benzene–alcohol yielded 4·4 g. of crystalline material, m. p. approximately 196°, which was fractionated from *cyclo*hexane by the triangle method, specific rotations being determined after every five crystallisations. The rotation of the least soluble fraction attained the constant value $[\alpha]_D^{17^\circ}$ − 10° (c = 1·025, l = 1) after fifteen crystallisations (m. p. 210—211°), but the m. p. still rose slowly, becoming constant at 215—217° after twenty-four crystallisations (Found: C, 71·2; H, 8·5. $C_{36}H_{52}O_6N_2$ requires C, 71·0; H, 8·6%). Hydrolysis of this *ester* yielded the free ε-sitosterol, m. p. 143—144°, $[\alpha]_D^{17^\circ}$ − 38·7° (c = 0·35, l = 1); the corresponding acetate separated from alcohol in plates, m. p. 127—128°, $[\alpha]_D^{17^\circ}$ − 44·7° (c = 0·645, l = 1).

From the more soluble dinitrobenzoate fractions a product was obtained having m. p. 207—209° and $[\alpha]_D^{17^\circ}$ − 21·7° (c = 1·20, l = 1), these values being unchanged by further crystallisation. The sterol, obtained by hydrolysis of this ester with 6% alcoholic potash, separated from alcohol in plates, m. p. 135—135·5°, $[\alpha]_D^{17^\circ}$ − 34·2° (c = 1·96, l = 1). The acetate, prepared in the usual manner, melted at 126—127° (124—125° when mixed with ε-sitosteryl acetate) and had $[\alpha]_D^{17^\circ}$ − 34·7° (c = 1·105, l = 1); the corresponding benzoate (plates from acetone) had m. p. 145—146° and $[\alpha]_D^{17^\circ}$ − 14·2° (c = 0·94, l = 1). The values recorded by Ichiba (*loc. cit.*) for derivatives of β-sitosterol are m. p. 136—137° and $[\alpha]_D$ − 31·5° for the free sterol, 122—123° and − 36·7° for the acetate, and 146—147° and − 12·3° for the benzoate.

Fraction F.—This was treated as described for fraction C, a small amount of substance X being isolated from the water-soluble material after benzoylation (m. p. 123°; crystallised from ether–ligroin).

Paraffin Fraction from Mexican Sarsaparilla Root.—The root was extracted and the saponins and free acids were removed as already described. The neutral fatty material (400 g.) was dissolved in alcohol–ether (8 : 1, 900 c.c.) and the crystalline product (47 g.) which separated was refluxed for 3 hours with 10% alcoholic potash (500 c.c.). The non-saponifiable fraction (24 g.), isolated by the usual method, was dissolved in warm acetone; on cooling, 2·25 g. of crystalline material separated, m. p. 70—70·5° after recrystallisation (Found: C, 85·8; H, 14·0%; *M*, 347). A solution of this mixture (1·55 g.) in chloroform (100 c.c.), light petroleum

(100 c.c.), and benzene (60 c.c.) was filtered through a column of alumina (Merck's "standardisiert nach Brockmann"). The filtrate contained a paraffin fraction, m. p. 61—62° after crystallisation from acetone (Found: C, 85·4; H, 14·7; *M*, 318. $C_{23}H_{48}$ requires C, 85·1; H, 14·9%; *M*, 324).

The chromatogram was developed with chloroform–benzene (75 c.c., 1 : 1); the material in the filtrate had m. p. 76—79° and was clearly a mixture. The column was then divided into three sections of equal length, each of which was eluted with light petroleum–methyl alcohol. The middle and bottom zones gave products of identical m. p. 80—81°, which were combined and recrystallised from acetone without change in the m. p. (Found: C, 82·6; H, 14·1%; *M*, 386). This substance was readsorbed on alumina; the filtrate both before and after development contained only traces of material, the bulk of the *compound* being recovered by elutriation of the middle section of the column. It crystallised from acetone in small plates, m. p. 82—82·5°. It was recovered unchanged after refluxing both with semicarbazide acetate in alcohol and with acetic anhydride, and after heating with 3 : 5-dinitrobenzoyl chloride in pyridine (Found: C, 80·2; H, 13·7. $C_{20}H_{42}O$ requires C, 80·4; H, 14·2%).

The elutriate from the top section of the first adsorption-column crystallised from acetone in small nodules, m. p. 102—104° (Found: C, 76·3; H, 12·6; *M*, 514. $C_{29}H_{56}O_3$ requires C, 76·6; H, 12·9%; *M*, 454). The *compound* gives no coloration with tetranitromethane.

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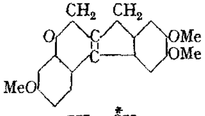
148. *Experiments on the Synthesis of Brazilin and Hæmatoxylin. Part V.*

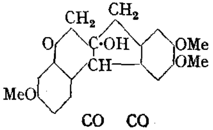
By H. APPEL, WILSON BAKER, H. HAGENBACH, and ROBERT ROBINSON.

THREE methods have been developed for the synthesis of substances containing the brazilane skeleton, and these lead to α-pyrones (Prescott and Robinson, 1911), to pyrylium salts (Crabtree and Robinson, 1918, 1922) or to γ-pyrans (Perkin, Ray, and Robinson; Pfeiffer and collaborators, 1912—), which are all closely related to brazilin. In the last two methods, actual brazilin derivatives have been synthesised; such are trimethoxybrazylium salts, anhydrotrimethylbrazilin (I), trimethylbrazilone, and their hæmatoxylin analogues. In spite of attempts repeated at intervals during the last fifteen years, it has not been found possible to extend any of these methods so as to accomplish the synthesis of trimethylbrazilin (II) itself, and in particular the hydration of (I) could not be effected, chiefly because it is itself the base of quinonoid oxonium salts and furthermore it is converted with remarkable ease into trimethoxybrazylium salts in the presence of acids or by means of the halogens or their equivalents.

It seems likely that the substance (III) isomeric with anhydrotrimethylbrazilin (I) would exhibit the normal character of an indene and show far less tendency than (I) to pass into a quinonoid-oxonium or pyrylium salt. We have to take the risk of indene tautomerism between the two forms; it is not certain that the system will be a mobile one. Hence we have directed attention to methods of preparation of intermediates in the synthesis of substances in which the asterisked position in (III) represents a carbonyl group. Full

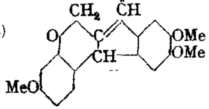
(I.)

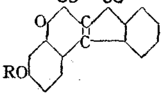




(II.)

(III.)



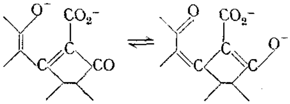


(IV.)

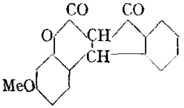
reduction of such an intermediate should yield an isomeride of (II), from which (III), and then (II), might be accessible.

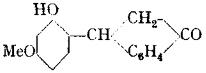
Two promising lines of investigation have been opened up in this direction and it is hoped to pursue both of them beyond the point reached in the present communication.

The condensation of ethyl 1 : 3-indanedione-2-carboxylate with resorcinol could only be brought about by means of hydrogen chloride in alcoholic solution (cf. Appel, J., 1935, 1031) and it then afforded a *coumarin* derivative (IV, R = H). This intensely yellow substance dissolves in aqueous sodium carbonate to a red solution, but in aqueous sodium hydroxide to a deep blue solution. Its *methyl* ether (IV, R = Me) is also yellow and gives a blue solution in alcoholic sodium hydroxide. The blue colour is therefore probably a manifestation of the *o*-hydroxyphenylindone structure in alkaline solution and the true explanation of the deep colour of salts of unsaturated hydroxy-ketones in general will apply to this particular case. The tautomerism, distribution of anionic charge, or resonance which is here possible may be represented by the expression :



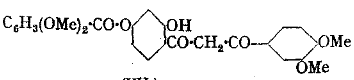
On reduction with zinc and acetic acid, IV (R = Me) yields a *dihydro*-derivative, which is probably (V), and with zinc and aqueous sodium hydroxide a phenolic *ketone*, $C_{16}H_{14}O_3$, regarded as having the constitution (VI), is produced.

(V.) 

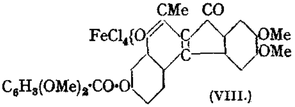
 (VI.)

Experiments on the condensation of (VI) with formaldehyde derivatives give promise of realisation of the first part of the general scheme outlined above and this work is in progress; the analogous series starting with *m*-hemipinic acid instead of phthalic acid will also be studied.

A remarkably facile synthesis of the brazilin skeleton has been encountered in the further examination of ω-veratroylresacetophenone 4-veratrate (VII) (Baker, J., 1933, 1387). When this substance is suspended in acetic anhydride and treated at room temperature with zinc chloride, stannic chloride, or ferric chloride, an intensely orange-red solution is at once obtained and eventually bright red oxonium salts separate unless very low concentrations have been employed. With each of the three metallic chlorides the products are double salts which could not be recrystallised without decomposition; the zincichloride was not obtained in a pure state, but the analyses of the *stannichloride* pointed to the formula $(C_{28}H_{23}O_8)_2SnCl_6$ and those of the *ferrichloride* to the formula $C_{28}H_{23}O_8FeCl_4$. It was apparent, therefore, that the veratroyloxy-group had not been eliminated and that the condensation, if regarded as one between diveratroylresacetophenone, acetic acid, and hydrogen chloride, involved the loss of $3H_2O$.



(VII.)



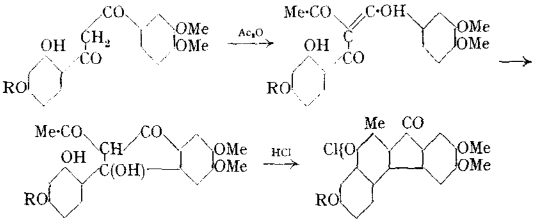
(VIII.)

Bearing in mind the syntheses of brazylium salts from homoveratrylpæanol (Crabtree and Robinson, J., 1918, 113, 859; cf. Baker and Robinson, J., 1925, 127, 1424, for the behaviour of homoveratrylresacetophenone) by the combined action of acetic anhydride

and zinc chloride, the brilliant red colour of the salts, and the above-mentioned analyses, it seemed very probable that they were ketohomobrazylium derivatives (VIII for the ferrichloride). This was confirmed by permanganate oxidation, which afforded veratric (from the veratroyloxy-group) and *m*-hemipinic acids.

The salts differ from the trimethoxybrazylium derivatives in that they are derived from a very weak base and in their lack of fluorescent properties. This is in accord with analogy; the direct union of the pyrylium nucleus with a carbonyl group should impair the basic function, and the non-fluorescent character of the 3-acylflavones may also be recalled in this connection.

The mechanism of the conversion of (VII) into (VIII) may be briefly considered and the chief point to note is that any satisfactory theory must include an explanation of the attack on the veratroyl nucleus, which is apparently inactivated by union with a carbonyl group. Ring-closures, such as that of benzoylbenzoic acid to anthraquinone, in the *o*-position to a keto-group are seldom accomplished with great ease and in the present case we suggest that enolisation prior to ring-closure must be assumed to occur. That reactions of this type do not proceed by way of intermediate chromones and that therefore the indene ring closure precedes that of the pyran nucleus has been demonstrated in similar cases (Baker and Robinson, *loc. cit.*) and reasons have been given for believing that *o*-hydroxydibenzoylmethanes can be directly *C*-acylated (Baker, *loc. cit.*). Hence the most probable course of the reaction is that represented in the following scheme:

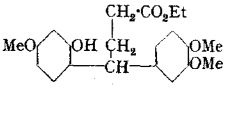


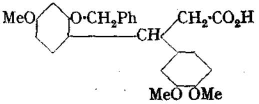
O-Veratroylpæanol undergoes rearrangement with far less readiness than *O*-diveratroylresacetophenone, but a 70% yield of *ω-veratroylpæanol* is obtainable by the use of sodamide instead of potassium carbonate (cf. Mahal and Venkataraman, *Current Science*, **1933**, **2**, 214; J., **1934**, 1767; Bhalla, Mahal, and Venkataraman, J., **1935**, 868). ω-Veratroylpæanol evidently undergoes a reaction of the type discussed above, but the products do not crystallise from the solutions and so could not be isolated in a pure condition.

Attempts to employ formic acid, ethyl formate, or ethyl orthoformate in these reactions were not successful, but it is not improbable that a salt of the type (VIII) (zincichloride) could be reduced and hydrolysed with the formation of a ketone constituted like (VI), and further work will be directed to this end.

Some other possible methods of attack on this synthetical problem have been explored in a preliminary fashion. 7-Hydroxy-4-veratrylcoumarin (Mitter and Paul, *J. Indian Chem. Soc.*, **1931**, **8**, 271) has been successively methylated, reduced, hydrolysed, and esterified with formation of *ethyl β-veratryl-β-(2-hydroxy-4-methoxyphenyl)propionate* (IX), but this ester could not be condensed with ethyl formate. Also the benzyl ether of the corresponding acid (X) could not be dehydrated to a hydrindone derivative.

(IX.)





(X.)

Experimental.

7-Hydroxy-1'-ketoindeno(2' : 3' : 3 : 4)*coumarin* (IV, R = H).—Cold saturated alcoholic hydrogen chloride (100 c.c.) was gradually added, during ½ hour, to a well-cooled and agitated mixture of resorcinol (60 g.), alcohol (300 c.c.), and ethyl indanedionecarboxylate (20 g.; Wislicenus, *Ber.*, 1887, **20**, 593). Complete solution occurred after 20 minutes and the yellow product began to crystallise after 1 hour; it was collected after 12 hours, washed with alcohol and acetone, and dried (10·2 g., sufficiently pure for most purposes). The *indenocoumarin* is sparingly soluble in most organic solvents and crystallises from a large volume of aqueous acetone in orange-yellow needles, which do not melt at 340° (Found: C, 72·9; H, 3·4. $C_{16}H_8O_4$ requires C, 72·7; H, 3·1%). The solution in aqueous sodium carbonate is deep red and on the addition of 10 vols. of 10% aqueous potassium hydroxide the colour changes to intense pure blue in about 2 minutes. On acidification the unchanged substance is regenerated.

1'-Keto-7-methoxyindeno(2' : 3' : 3 : 4)*coumarin* (IV, R = Me).—The foregoing phenol cannot be conveniently methylated by means of methyl sulphate and alkali. Methyl iodide (50 c.c.) was added to a mixture of hydroxyketoindenocoumarin (7·5 g.), silver oxide (20 g.), and methyl alcohol (150 c.c.), and the mixture refluxed until a sample did not give a red colour on addition to aqueous sodium carbonate (15—30 minutes). After cooling, the solids were collected and extracted (Soxhlet) with acetone. The *methyl* ether separated during the extraction and was collected (7·0 g.); it crystallised from acetone in small, rectangular, orange-yellow plates, m. p. 270° (Found: C, 73·3; H, 3·7. $C_{17}H_{10}O_4$ requires C, 73·4; H, 3·6%). This methyl ether is somewhat more readily soluble in the usual organic solvents than the parent phenol; it is insoluble in aqueous alkalis. The solution in alcoholic sodium ethoxide is deep blue; on the addition of a little water this changes to red and on further dilution the yellow indenocoumarin separates. This formation of the lactone in alkaline solution is noteworthy.

When zinc dust was added in small portions to a boiling solution of ketomethoxyindenocoumarin (1 g.) in acetic acid (40 c.c.), a colourless liquid was obtained; this became yellow again on shaking with air. If the colourless solution was expeditiously filtered and added to water, the *dihydro*-derivative (V) was obtained as a colourless precipitate (yield, quantitative). The substance suffers rapid autoxidation in solvents in the presence of air; a quick crystallisation from alcohol afforded slightly yellowish needles, m. p. 185—187° after turning yellow and softening at 180° (Found: C, 72·6; H, 4·6. $C_{17}H_{12}O_4$ requires C, 72·8; H, 4·3%). Microscopic examination of a specimen crystallised from ethyl acetate disclosed a mixture of needles of the dihydro-derivative and yellow rectangular plates of the ketomethoxyindenocoumarin.

2'-Hydroxy-4'-methoxy-3-phenylindan-1-one (VI).—Sodium hydroxide (200 c.c. of 5%) was added to a mechanically stirred, boiling solution of ketomethoxyindenocoumarin (4 g.) in 50% alcohol (400 c.c.); the colour changed from red to intense violet. Under the same conditions zinc dust (about 50 g.) was added in small portions until the solution became colourless (about 1 hour). The filtered solution was acidified with hydrochloric acid, and the *product* isolated by means of ether. 3·2 G. crystallised on concentration of the extract to a small volume. The substance was thrice crystallised from alcohol and obtained in colourless rectangular prisms, m. p. 141·5° (Found: C, 75·7; H, 5·4. $C_{16}H_{14}O_3$ requires C, 75·6; H, 5·5%). The phenolic function is shown by the insolubility of the substance in aqueous sodium carbonate and the ready solubility to a colourless solution in aqueous sodium hydroxide.

The *semicarbazone*, prepared in cold aqueous alcoholic solution, crystallised from alcohol in small hexagonal plates, m. p. 213—214° (Found: C, 65·6; H, 5·6; N, 13·3. $C_{17}H_{17}O_3N_3$ requires C, 65·6; H, 5·5; N, 13·5%). An oxime was also prepared but not completely purified; m. p. 75—77° after precipitation from aqueous ammoniacal solution by means of acetic acid. The *methyl* ether, obtained by the action of methyl sulphate on a solution of the phenolic ketone in 20% aqueous sodium hydroxide, crystallised from alcohol in slender needles, m. p. 89° (Found: C, 75·7; H, 5·9. $C_{17}H_{16}O_3$ requires C, 76·1; H, 6·0%).

Condensation of the phenolic ketone with ethyl formate and powdered sodium afforded a small quantity of a red substance, very sparingly soluble in alcohol. After washing with hot alcohol this had m. p. 184—185° and appeared to have the composition of a hydroxymethylene derivative (Found: C, 72·2; H, 4·7. $C_{17}H_{14}O_4$ requires C, 72·3; H, 5·0%). The quantity obtained was insufficient to enable us to make a more complete investigation.

2-Hydroxy-4 : 3' : 4'-trimethoxybenzophenone.—Powdered aluminium chloride (16 g.) was added to a mixture of veratroyl chloride (16 g.), resorcinol dimethyl ether (11 g.), and carbon disulphide (25 c.c.). After the reaction had subsided, the mixture was refluxed for 1 hour. The *product* was crystallised from alcohol (yield, 14·0 g.); m. p. 140—141° (Found: C, 66·8; H, 5·5; MeO, 32·0. $C_{16}H_{16}O_5$ requires C, 66·6; H, 5·6; 3MeO, 32·3%). The phenolic hydroxyl

(strong ferric reaction) remained unaffected when the substance was treated with chloroacetic acid or β-chloropropionic acid in alkaline solution or with ethyl diazoacetate; in all cases a variety of conditions was tried.

Ethyl Veratroylacetate.—By a slight modification of Claisen's method for the preparation of ethyl benzoylacetate, veratroyl chloride (40 g.) afforded 35 g. of the ester. Mitter and Paul (*loc. cit.*) obtained it as an oil; our product crystallised, m. p. 37·5—39·5°, after being washed with a little chilled alcohol. The ferric reaction in alcoholic solution is brown-red and appears only in the course of a few seconds; hence the solid is the keto-modification (Found: C, 61·8; H, 6·5. Calc. for $C_{13}H_{16}O_5$: C, 61·9; H, 6·4%).

7-Hydroxy-4-veratrylcoumarin.—The method of Mitter and Paul (*loc. cit.*) gives a poor yield. Under the following conditions the yield is 90%. An ice-cooled mixture of ethyl veratroylacetate (2·5 g.), resorcinol (5·5 g.), and alcohol (25 c.c.) was saturated with hydrogen chloride and kept for 20 hours. The product obtained on the addition of water was crystallised from alcohol (yield, 2·7 g.); m. p. 233—235° (Found: C, 68·7; H, 4·9. Calc. for $C_{17}H_{14}O_5$: C, 68·4; H, 4·7%).

7-Methoxy-4-veratrylcoumarin.—Methyl sulphate (60 c.c.) was added to a stirred solution of hydroxyveratrylcoumarin (10 g.) in aqueous potassium hydroxide (500 c.c. of 1%). Any excess of methyl sulphate was destroyed by the addition of small quantities of concentrated potash. The yield of recrystallised product was 7·4 g., and 0·5 g. was obtained from the mother-liquors. This coumarin derivative occurs in two forms: long thin prisms, m. p. 151—153°, and short stout prisms, m. p. 161—163°. The latter form is the more sparingly soluble and has been previously described by Mitter and Paul (*loc. cit.*). The more fusible variety, not mentioned by these authors, crystallises from hot concentrated alcoholic solutions (Found in material of m. p. 151—153°: C, 69·3; H, 5·2. $C_{18}H_{16}O_5$ requires C, 69·2; H, 5·2%).

7-Methoxy-4-veratryldihydrocoumarin.—A solution of sodium ethoxide (0·5 g. of sodium) in alcohol (25 c.c.) was added to a boiling one of 7-methoxy-4-veratrylcoumarin (2 g.) in alcohol (25 c.c.); a sodium salt soon separated from the yellow liquid. Water (25 c.c.) was added, and reduction effected by means of sodium amalgam (80 g. of 3%). The acid was liberated and isolated by extraction with ethyl acetate (A). The residue after evaporation of the dried extract was heated in a vacuum at 120°, and an alcoholic solution of the product allowed to evaporate at the room temperature. Crystals separated and these were purified by solution in ethyl acetate and slow evaporation; finally the *product* was washed with a little cold alcohol; m. p. 82—83° (Found: C, 68·6; H, 5·8. $C_{18}H_{18}O_5$ requires C, 68·8; H, 5·8%).

Ethyl β-Veratryl-β-(2-hydroxy-4-methoxyphenyl)propionate (IX).—The residue (A) above was refluxed for 2½ hours with alcohol (100 c.c.) and sulphuric acid (0·5 c.c.). The resulting *ester* was isolated by means of ether and crystallised in contact with a little alcohol; it was recrystallised from aqueous alcohol, m. p. 113—115° (yield, 1·65 g.) (Found: C, 66·8; H, 6·6. $C_{20}H_{24}O_6$ requires C, 66·6; H, 6·7%).

β-Veratryl-β-(2-benzyloxy-4-methoxyphenyl)propionic Acid (X).—A mixture of the foregoing ester (3·6 g.), benzyl chloride (5·2 g.), potassium carbonate (5·6 g.), potassium iodide (0·5 g.), and acetone (10 c.c.) was refluxed for 7 hours. Potassium hydroxide (20 g.) in 50% alcohol (120 c.c.) was then introduced, and the mixture boiled for 2 hours; during the second hour alcohol was allowed to evaporate. Water was added, and the solution shaken with ether; when the aqueous layer was cautiously acidified in the presence of a little sulphur dioxide, the *acid* soon separated in a crystalline condition (yield, quantitative). The substance may be purified by conversion into its sparingly soluble sodium salt and by crystallisation from aqueous alcohol or ethyl acetate–light petroleum. The crystals, m. p. 95°, contain approximately $1H_2O$; after drying at 50° in a high vacuum the m. p. was 104—105° (Found in anhydrous material: C, 71·2; H, 6·4. $C_{25}H_{26}O_6$ requires C, 71·1; H, 6·2%). Attempts to effect ring-closure of this acid were made in several ways, but in most cases there was evidence of hydrolysis of the benzyloxy-group and no hydrindone derivative could be isolated.

As shown above, our objective has meanwhile been reached along other lines, so this route has been abandoned.

ω-Veratroylresacetophenone 4-Veratrate (VII).—The constitution of this substance has been confirmed by hydrolysis. It was boiled with dilute aqueous sodium hydroxide for a few minutes and the resulting solution was extracted with ether. Acetoveratrone was thus isolated, m. p. 48° alone or mixed with an authentic specimen.

7-Veratroyloxy-3′ : 4′-dimethoxyflavone.—A solution of ω-veratroylresacetophenone 4-veratrate (1 g.) in acetic acid (15 c.c.) was saturated with hydrogen chloride. After 1 hour the orange-yellow oxonium salt was collected, washed with acetic acid, decomposed by stirring

into water, collected, and dried. After recrystallising twice from acetic acid, it formed colourless microscopic prisms, m. p. 219° (Found in material dried at 100° in a vacuum over sodium hydroxide: C, 67·3; H, 4·7. $C_{26}H_{22}O_8$ requires C, 67·6; H, 4·7%). The solution in a mixture of chloroform and alcohol shows a marked blue fluorescence.

9-Keto-7-veratroyloxy-4′ : 5′-dimethoxybrazylium Zincichloride (related to VIII).—ω-Veratroylresacetophenone 4-veratrate (0·5 g.) was added to a mixture of acetic anhydride (1 c.c.) and powdered anhydrous zinc chloride (0·5 g.). Complete solution occurred in about 5 minutes with production of an intense orange-red colour. After 12 hours the solution was saturated with hydrogen chloride, and after a further 24 hours the crystalline material was collected on a porous tile. It separated from boiling acetic acid (20 c.c.), containing a little hydrogen chloride, in bright red, minute, prismatic needles [Found: C, 55·7; H, 4·4; Cl, 10·3; Zn—residue of ZnO, 6·3. $(C_{28}H_{23}O_9)_2ZnCl_4$ requires C, 56·9; H, 3·9; Cl, 12·0; Zn, 5·5%].

The Stannichloride (related to VIII).—A freshly prepared 10% solution of stannic chloride in acetic anhydride (12 c.c.) was added to ω-veratroylresacetophenone 4-veratrate (2 g.) with instantaneous production of a brilliant red solution. The *stannichloride* began to separate in about 2 hours, and after about 12 hours was collected, washed with acetic acid and then benzene, and dried (yield, 2·5 g.). It formed microscopic, purplish-red crystals [Found: C, 48·1; H, 3·6; Cl, 19·3; Sn as residue, 10·9. $(C_{28}H_{23}O_8)_2SnCl_6,2HCl$ requires C, 48·7; H, 3·5; Cl, 20·6; Sn, 8·6%]. The compound may be crystallised with difficulty and in small quantity from acetic acid containing a little stannic chloride. When it is boiled with water, a tin-containing ochre-yellow powder is produced; when heated with dilute hydrochloric acid, it gives a tin-free black powder, which shows signs of being converted into an oxonium salt on treatment with hydrogen chloride in acetic acid.

The Ferrichloride (VIII).—ω-Veratroylresacetophenone 4-veratrate (0·5 g.) was added to a solution of anhydrous ferric chloride (0·25 g.) in acetic anhydride (3 c.c.). After 12 hours the dark brownish-red solution had become a pasty crystalline mass, which, after being pressed on porous earthenware, left a mass of rather dark purplish-red, microscopic crystals. When these were warmed with a little acetic anhydride, a dark solution was obtained, but almost immediately the *ferrichloride* crystallised in bright red, microscopic needles. The substance was collected, washed with acetic acid, then with benzene, and dried for ½ hour at 100° (Found, in two different specimens: C, 49·5, 49·6; H, 3·5, 3·9; Fe, 10·2, 7·8; Cl, 18·1. $C_{28}H_{23}O_8FeCl_4$ requires C, 49·1; H, 3·4; Fe, 8·2; Cl, 20·7%).

Oxidation to m-*Hemipinic Acid*.—Powdered potassium permanganate (7 g.) was added in small quantities at a time to a solution of the stannichloride (1·5 g.) in pyridine (20 c.c.) and water (20 c.c.). The mixture was shaken and warmed; towards the end of the oxidation more water was added and the mixture heated more strongly. Sulphur dioxide was then passed in excess, the hot solution extracted thrice with ethyl acetate, and the extracts dried with sodium sulphate and distilled, leaving a mainly crystalline residue. This was found to be incompletely oxidised, so it was again treated with warm aqueous potassium permanganate and a little sodium hydroxide, and the acidic product again collected as before. The crystalline residue was boiled twice with water (the filtrate, after treatment with charcoal and evaporation to a small bulk, deposited veratric acid in fine needles, m. p. and mixed m. p. with an authentic specimen, 179°), the remaining solid dissolved in an aqueous solution of ethylamine, the solution evaporated to dryness, and the residue distilled. The yellowish crystalline material separated from alcohol, in which it was very sparingly soluble, in very fine prisms, m. p. 225—226° (Found: C, 61·1; H, 5·7. Calc. for $C_{12}H_{13}O_4N$: C, 61·3; H, 5·6%). A genuine specimen of *m*-hemipinethylimide had m. p. 227°, and a mixed m. p. of the two specimens was 225—226°. The specimens were indistinguishable in their crystalline form, and both exhibited the same weak bluish-green fluorescence in alcoholic solution.

Pæanol.—Methyl sulphate (96 g.; 1·1 mols.) was added during 2 hours at room temperature to a stirred solution of crude resacetophenone (105 g.) in water (300 c.c.) containing sodium hydroxide (30·5 g.; 1·1 mols.) and methyl alcohol (200 c.c.). The mixture was slowly heated on the steam-bath for a further 2 hours with continuous stirring, most of the alcohol being allowed to distil during the last hour. The mixture was made faintly alkaline to litmus by the addition of a little sodium hydroxide and cooled in ice, and the solid pæanol collected, washed thoroughly with water, dried, and distilled; b. p. 154°/20 mm. (yield, about 60 g.).

O-*Veratroylpæanol*.—A mixture of pæanol (26·5 g.), veratroyl chloride (32 g.) and pyridine (50 c.c.) was heated on the water-bath for ½ hour, and poured into dilute hydrochloric acid. The colourless crystalline product was collected, washed with dilute hydrochloric acid, then

water, stirred into a large volume of cold alcohol, collected, and dried at 100° (yield, 34 g.). This *product* is sufficiently pure for the succeeding step. For analysis it was crystallised first from benzene–alcohol, then ethyl acetate, and finally acetone; it formed minute colourless needles, m. p. 158—159° (Found: C, 65·3; H, 5·5. $C_{18}H_{18}O_6$ requires C, 65·4; H, 5·5%).

ω-*Veratroylpæanol*.—Sodamide (5 g.) was finely powdered under a little toluene and transferred with the help of more toluene (in all, 100 c.c.) to a flask containing *O*-veratroylpæanol (10 g.). The yellow sodium salt of ω-veratroylpæanol began to appear at once in the cold, and increased rapidly in amount when the flask was heated on the water-bath for 4 hours with frequent shaking, ammonia being abundantly evolved. The yellow solid (containing some unchanged sodamide!) was collected, washed with hot benzene, dried on the water-bath, and stirred cautiously into cold water; the solution was acidified with hydrochloric acid, and the yellow solid collected, washed, and dried on the water-bath (yield, 7 g.). It separated from about 5 times its weight of benzene in pale yellow, extremely fine prisms, m. p. 162—163° (Found: C, 65·4; H, 5·7. $C_{18}H_{18}O_6$ requires C, 65·4; H, 5·5%).

When treated in acetic anhydride with zinc chloride, stannic chloride, or ferric chloride, this *compound* gives brilliant red solutions exactly resembling those given by ω-veratroylresacetophenone 4-veratrate, but the pyrylium salts do not separate on standing. Unlike the diveratroyl compound, ω-veratroylpæanol is not converted into a flavone derivative by treatment with hydrogen chloride in acetic acid; no oxonium salt separates, and the substance is recovered unchanged by pouring into water.

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149. *The Kinetics of the Reaction between Oxygen and Sulphur. Part II. The Frigescent Oxidation of Sulphur.*

By Leonard A. Sayce.

It has been shown (Part I; Sayce, J., 1935, 1767) that saturated sulphur vapour and oxygen between 50 and 400 mm. and 200° and 280° react on quick cooling, producing in this rapid " frigescent " reaction more sulphur dioxide than is formed during long periods of steady heating at the same temperature range. The phenomenon is frequently accompanied by a flash of light. The normal slower reaction taking place at 240—280° has already been studied (see Part I) by adopting an experimental technique for circumventing the frigescent reaction, the detailed investigation of which is now described.

Visible reaction occurs only in presence of condensed sulphur which has been rapidly cooled to approx. 160° and is due to the explosion of sulphur vapour and oxygen at this temperature. The explosion appears to be initiated by energy liberated in a transition in the liquid sulphur, a portion of which is itself oxidised, and to occur only when this is liberated suddenly after a hysteresis resulting from rapid cooling. This hypothesis is supported by the fact that the reaction is suppressed by small amounts of iodine and chlorine, the former of which profoundly affects the physical properties of sulphur at about this temperature by an interference in the transition $\lambda S \rightleftharpoons \mu S$.

Experimental.

The experimental work was done in Pyrex glass, for the most part in sealed bulbs of 50—100 c.c. capacity. The sulphur used was carefully purified (Aynsley and Robinson, *Chem. and Ind.*, 1935, **54**, 392), weighed on a microbalance, and dispersed uniformly over the walls of the vessels by sublimation in a vacuum. The oxygen, generated by electrolysis of dilute sulphuric acid and freed from traces of acid spray, hydrogen, and ozone, was passed over potassium hydroxide and phosphoric oxide before use. The charged bulbs were heated in a thermostatic oil-bath, and after the prescribed treatment the amount of sulphur dioxide formed was estimated by opening them under 0·001*N*-iodine. More than a trace of the trioxide was found only in exceptional cases. As was anticipated from the earlier work, a high degree of concordance between the individual results was not obtained, and for that reason experiments were normally repeated several times.

Influence of Initial Temperature.—Bulbs containing saturated sulphur vapour and oxygen at 180×10^{-6} g. per c.c. (equivalent to a pressure of approx. 100 mm. Hg at 15°) were heated

for 5 mins. at $T°$ and allowed to cool, in the air, to room temperature. From the sulphur dioxide formed (see below), it is evident that for sulphur to take part in the frigescent reaction it must have been above an initial temperature of 200°, and further, that the maximum reaction is attained when it has been heated to approximately 220°.

T	180°	190°	200°	210°	220°	230°
SO_2 yield per 100 c.c. (g. × 10^{-6}) ...	17·6	12·5	40·0	838	3240	2912

Influence of Sulphur Concentration.—Bulbs containing the above concentration of oxygen and various amounts of sulphur were heated at 250° for 5 minutes and cooled as before. In Table I are recorded the sulphur concentration, yield of sulphur dioxide (g. × 10^{-6}), the temperature ($T°$) at which the sulphur vapour became saturated, and the cooling period (P secs.) after which the flash, if any, occurred. Two features emerge: (i) that there is no visible inflammation and appreciably less sulphur dioxide is produced when the sulphur vapour reaches saturation below a specific temperature, *ca.* 174°, and (ii) that when saturation is reached above this temperature the probability of incandescence is high, and although the amounts of sulphur dioxide vary somewhat they range about a constant figure and are not greatly altered by a considerable excess of sulphur. The period after which the flash takes place is fairly uniformly 55 secs., pointing to a critical temperature at which incandescence is initiated. It is notable that the flash is always seen *after* the appearance of condensed sulphur upon the walls of the reaction vessel.

TABLE I.

Expt. No.	1	2	3	4	5	6	7	8	9	10	11	12
S, mg.	0·236	0·382	0·417	0·624	0·651	1·024	1·038	1·14	1·36	2·10	3·01	3·36
SO_2 yield (g. × 10^{-6})	0·0	208	288	512	864	1440	1506	1472	944	2114	1792	1840
T	154°	160°	164°	173°	174°	185°	186°	188°	192°	203°	214°	217°
P	Nil	Nil	Nil	Nil	58	54	51	56	59	58	52	51
Expt. No.	13	14	15	16	17	18	19	20	21	22	23	
S, mg.	3·72	3·99	4·11	4·38	4·54	4·71	5·01	5·93	6·75	10·00	12·40	
SO_2 yield (g. × 10^{-6})	2560	2175	1569	2115	1218	2337	2369	1378	1137	2210	3135	
T	220°	222°	223°	225°	226°	227°	229°	234°	239°	253°	260°	
P	47	64	58	74	56	46	47	Nil	Nil	60	51	

Temperature of Bulb at which Flash Occurs.—Bulbs fitted with thermocouples of low heat capacity constructed of fine chromel-eureka wires thinly coated with glass, and with the junction situated either at the centre or touching the wall, were charged with excess of sulphur and oxygen as before, heated to 250°, and allowed to cool in air. The mean temperature at which flashing occurred was found to be 170° irrespective of the position of the junction. By applying to the flash intervals, P, of Table I a cooling curve obtained with a typical bulb, the apparent mean temperature of flashing of the 23 cases was found to be 172°. Thermocouples of bare wire gave temperatures a few degrees lower, and there is reason to believe that an allowance of about 10° must be made on the above figures for the heat capacity of the couple and the lag of the galvanometer, so the true mean temperature of the reactants at which flashing occurs is approx. 160°. Hence, since no flashing occurs in bulbs in which the sulphur reaches saturation below about 174°, it is evident that it is consequent upon the presence of condensed sulphur.

Influence of Rate of Cooling.—It has already been shown (Part I, *loc. cit.*) that very slow cooling leads to the production of very small quantities of sulphur dioxide, and quick cooling in kerosene, water, or air to increasingly larger quantities. In the following experiments the range of temperature in which quick cooling is effective was investigated. Bulbs were placed in a bath at 240° for 5 minutes and quickly removed to a second bath at a lower temperature, wherein they were allowed to cool very slowly. Experience having shown negligible amounts of sulphur dioxide to be produced by such slow cooling, it follows that the sulphur dioxide found was mainly produced during cooling through the interval of temperature between the two baths. Individual results showed considerable variations, an occasional anomalously high yield of sulphur dioxide being obtained at each temperature; these anomalies being omitted, the means of many experiments gave the data recorded in Table II.

TABLE II.

Temp. of cooling bath	200°	180°	170°	160°	150°	145°	140°	130°
Average yield of SO_2 per 100 c.c. bulb capacity (g. × 10^{-6})	66·0	76·0	80·5	83·2	424	789	1479	2490

With rapid cooling to below 160°, the temperature at which flashing occurs, the yield rises

suddenly and continues to increase as the temperature drop is increased: this is believed to be due to a greater speed of cooling more favourable to hysteresis in the transition of μS to λS (see later).

Influence of Local Cooling.—An hour-glass-shaped bulb, containing sulphur and oxygen at the above concentrations and having a narrow constriction between its two chambers, was completely immersed in oil at 250° for 5 mins., after which the upper portion was drawn out of the bath until the constriction was level with the surface of the oil. After 48 secs., and in a second experiment 110 secs., a very brilliant flash occurred, filling both chambers of the bulb and accompanied by a distinctly audible click. Evidently, the frigescent reaction is initiated in the cooler part of the system, whence it spreads homogeneously. The especial brilliancy of the flash in these experiments is ascribable to the concentration of sulphur vapour maintained in the heated portion of the bulb.

That the flash of the frigescent reaction is, in fact, an explosion of sulphur vapour and oxygen was shown in another way. A bulb furnished with an internal spark-gap of tungsten wire and containing the two reactants was heated gradually in an oil-bath, a spark from an induction coil being passed across the gap at intervals of about 5°. The temperatures at which an explosion was seen to occur lay between 142° and 150°, mean 146°. If the spark was delayed until a higher temperature and a correspondingly higher concentration of sulphur vapour had been reached, the brilliancy of the flash was increased, and even at 250° the mixture exploded vigorously, showing that it was still much below the upper critical explosion limit.

Influence of Iodine and Chlorine.—Bulbs containing sulphur and oxygen as before and, in some cases, small amounts of iodine were heated to 240° and cooled in the atmosphere. The results (below) show that iodine to the extent of 1—3% of the sulphur is enough entirely to

S, mg.	4·145	3·102	3·483	4·883	3·710	5·499
Iodine, mg.	—	—	—	0·102	0·113	0·054
SO_2 yield (g. × 10^{-6})	1229	1033	1182	68	78	78
Flash after, secs.	40	51	45	—	—	—

inhibit the reaction, such sulphur dioxide as was formed in bulbs containing iodine being entirely attributable to oxidation during the period of initial heating. High accuracy is not claimed for the amounts of iodine which were weighed into the reaction bulbs, since its appreciable vapour pressure led to some loss on evacuation.

The effect of lower concentration of halogen was conveniently studied by mixing chlorine with pure oxygen in a storage bulb and introducing the mixture into the reaction bulbs which were heated to 240° for 5 mins. and cooled in air. Each column in Table III represents the mean of several experiments: evidently chlorine behaves like iodine, since traces of it have a marked effect on the amount of sulphur dioxide produced, as little as 0·01 mg. per 100 c.c. sufficing to reduce the yield of sulphur dioxide to one-tenth.

TABLE III.

S, mg.	5·88	6·23	6·61	6·93	6·48	5·81
Cl, mg.	0	0·0098	0·0133	0·0365	0·231	0·714
S : Cl ratio	∞	635	496	190	28·0	8·13
SO_2 yield (g. × 10^{-6})	2432	240	215	134	42·5	11·8

It remained to be discovered whether the inhibition is upon the visible homogeneous reaction or upon the change in the condensed sulphur which initiates it. Experiments to observe the minimum temperature at which an electric spark ignites mixtures of oxygen and sulphur vapour, already described, were repeated in presence of various amounts of chlorine (Table IV), and it was found, within the limits of experimental error, to be unaffected by concentration of chlorine

TABLE IV.

Cl, %	0	0·013	0·035	0·093	0·59	1·6
Cl, mg. per 100 c.c.	0	0·00509	0·0137	0·0365	0·231	0·627
Min. temp. for explosion	142—150°	151°	152°	160°	170—180°	170—175°

up to 0·014 mg. per 100 c.c. At low concentrations chlorine does not impede the homogeneous reaction between sulphur and oxygen once it is started, and the observed inhibition (Table III) must be due to its effect upon the condensed sulphur. Concentrations of 0·2 mg. and more cause an increase in the minimum temperature for explosion (Table IV), and also reduce the yield of sulphur dioxide (Table III) below that expected from the initial heating at 240° (see above). As was subsequently demonstrated by direct experiment, chlorine at such concentrations also poisons the normal wall reaction described in Part I.

Discussion of Results.

Sulphur dioxide is produced in considerable quantities when mixtures of sulphur vapour and oxygen are cooled rapidly from temperatures over 210°, usually with the emission of a momentary flash of light. Once started by cooling a portion of the reaction vessel, the flash is capable of passing through a narrow tube into a region which is still uncooled, from which it appears that the particular reaction made visible by flashing is initiated by a cooling of the reactants and then proceeds homogeneously throughout the system. The production of sulphur dioxide is uninfluenced by the concentration of the sulphur, provided that this be more than sufficient to saturate the vapour when the reaction vessel is between 170° and 180°. With lower concentrations of sulphur there is no visible phenomenon accompanying the reaction, and the production of sulphur dioxide falls with diminishing sulphur content. The temperature of the vessel when flashing takes place is approximately 160°; hence, it depends on the presence of condensed sulphur. With very slow cooling the phenomenon is never observed, and even with rapid cooling it does not arise unless the range of rapid temperature change includes the region 150—160°. The temperature limit of 160°, above which the visible homogeneous reaction does not occur, might be attributable to an upper critical explosion limit to the reaction were it not that mixtures of saturated sulphur vapour and oxygen at the concentration used in the preceding experiments can be ignited electrically at all temperatures from 146° to 250°. If it be contended that the energy of ignition is greater when electrical means are employed than under the normal conditions of flashing, we have the experiments with the hour-glass-shaped bulb to prove that the homogeneous reaction initiated by cooling can, in fact, pass into a region where the concentration of sulphur is relatively high.

It is, therefore, to the film of sulphur condensing on the walls of the vessel at 160—170° and to its previous history that particular importance attaches: it must have been above 210° and must have cooled therefrom to 160° at a sufficiently rapid rate. It is known that there is a gradual transition of λS to μS when the element is heated above 150°, and that the reverse change shows a hysteresis so great as to allow the formation of "plastic sulphur." It is presumed that in the condensate the transition from μS to λS occurs gradually under conditions of very slow cooling, but that with quick cooling the energy of transition is liberated suddenly at *ca.* 160°. If this assumption be true, two alternative explanations are possible to account for the initiation of the visible homogeneous reaction. On the one hand, the gas reaction may be activated by the energy of transition, or, on the other hand, this energy may cause a local oxidation of the condensed sulphur which, in its turn, may provide the energy necessary to start the gas reaction.

Support is given to the latter explanation by the results in Table I. In a typical experiment the total yield of sulphur dioxide is made up of at least two distinct reactions. First, there is oxidation during the 5 mins.' preliminary heating period at 250° which, from the evidence of Part I, amounts to approximately 400×10^{-6} g. of sulphur dioxide per 100 c.c. Secondly, there is, in all but two of the later experiments, oxidation in the gaseous phase accompanied by flashing. But in the absence of the visible reaction there is evidence of a third reaction, for in Expts. 20 and 21 there was considerable oxidation producing about 1258×10^{-6} g. of sulphur dioxide. After deduction from this figure of the contribution made during the heating period, there remains 858×10^{-6} g. of sulphur dioxide, which, from the evidence of Table II, must have been made in the region of temperature where flashing normally occurs, presumably by oxidation of condensed sulphur, a presumption justified by the fact that the mean total yield of sulphur dioxide in Expts. Nos. 10—19 and 22 and 23, in which flashing occurred, surpasses the total yield of Nos. 20 and 21 by 862×10^{-6} g. of sulphur dioxide. This corresponds to the complete combustion of 100 c.c. of saturated sulphur vapour (assumed to be S_8) at 164°.

The effect of small amounts of iodine and chlorine in preventing oxidation also favours the hypothesis that it is initiated by a transition of μS to λS, for halogens have long been known to interfere with this transition. The quantities of chlorine which suffice to inhibit the reaction are too small to be effective by removing sulphur as sulphur chloride, and below 0·0365 mg. of chlorine per 100 c.c. neither the high-temperature wall reaction nor

the visible reaction is materially affected; yet as little as 0·01 mg. of chlorine per 100 c.c. prevents the visible reaction and reduces the total yield of sulphur dioxide to a tenth of its value with pure oxygen. It is believed that the inhibiting effect of chlorine operates upon the oxidation of condensed sulphur by affecting the transition which initiates it, and thereby denying the homogeneous reaction the necessary activation.

SUMMARY.

1. Mixtures of sulphur and oxygen of widely different compositions, when cooled rapidly from above 210°, react at *ca.* 160°.

2. The reaction is two-fold, and comprises the oxidation to sulphur dioxide of (*a*) condensed and (*b*) uncondensed sulphur. The latter is accompanied by the emission of light.

3. The first reaction is initiated by energy released in a transition in the liquid sulphur. There is reason to believe that the homogeneous reaction is activated by the oxidation of condensed sulphur rather than by the energy of transition.

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150. *Rottlerin. Part I.*

By ALEXANDER MCGOOKIN, FIRMIN P. REED, and ALEXANDER ROBERTSON.

THE main phenolic crystalline constituent of the Indian colouring matter and anthelmintic drug "kamala," which is obtained from the fruit glands of *Mallotus phillipinensis* (Muell) (synonym *Rottlera tinctoria*, Roxb.), appears to have been isolated first in 1855 by Anderson (*Edin. New Phil. J.*, 1, 296), who named the compound, $C_{11}H_{10}O_3$, rottlerin.* Although Leube (*Vierteljahrsschrift für prakt. Pharm.*, 1860, **9**, 319) and Oettingen (*Dissert.*, St. Petersburg, 1862) failed to obtain crystalline material from kamala, Anderson's results were amply confirmed by Perkin and Perkin (*Ber.*, 1886, **19**, 3109) and by Jawein (*ibid.*, 1887, **20**, 182), who gave m. p. 200° for rottlerin. The substance has been the subject of a number of investigations by several authors, but the results so far obtained have been somewhat contradictory [Perkin, J., 1893, **63**, 975; 1895, **67**, 230; 1899, **75**, 443, 829; Bartolotti, *Gazzetta*, 1894, **24**, (i), 1; (ii), 480; Telle, *Arch. Pharm.*, 1906, **244**, 441; Hermann, *ibid.*, 1907, **245**, 572; Dutt, J., 1925, **127**, 2044; Dutt and Goswani, *J. Indian Chem. Soc.*, 1928, **5**, 21; Hoffmann and Fari, *Arch. Pharm.*, 1933, **271**, 97] and accordingly a detailed summary of the work and conclusions of previous authors, which would not appear to be of special value at present, has been omitted from this memoir (see, however, Perkin and Everest, "Natural Organic Colouring Matters," London, 1918, p. 598, for a résumé of the results of Telle and earlier workers. It may be noted that the derivatives of phloroglucinol which Telle claims to have obtained from rottlerin were *C*-methyl compounds and not methyl ethers as quoted by Perkin and Everest, *loc. cit.*, and by Dutt, *loc. cit.*).

In the course of preliminary experiments it became evident that rottlerin is a highly reactive substance, difficult to obtain free from minute traces of accompanying impurities and unstable when heated with high-boiling solvents; *e.g.*, the use of toluene as a solvent for crystallisation purposes appears to cause slight resinification. Although an improved procedure for the preparation of the pure compound has been developed and the material has been obtained having a higher melting point, 212°, than that previously recorded, nevertheless in the case of rottlerin melting point alone cannot be regarded as an entirely satisfactory criterion of absolute purity. A considerable number of analyses of the com-

* The name mallotoxin suggested by Perkin and Perkin (*loc. cit.*) is more appropriate than rottlerin, but the latter has precedence and has been adopted in the literature.

pound have been carried out for us by Dr. A. Schoeller of Berlin and by Dr. Weiler of Oxford and though the results agree fairly well amongst themselves they do not permit us to make a final decision between the empirical formulæ $C_{33}H_{30}O_9$ and $C_{31}H_{30}O_8$ proposed by Perkin (*loc. cit.*) and by Hoffmann and Fari (*loc. cit.*) respectively. For the present we have employed Perkin's formula as a working hypothesis, since it appears to accord best with certain derivatives subsequently described, but further evidence from studies of the degradation products may well necessitate some modification of this formula.

Acetylation of rottlerin by the pyridine method at room temperature gave an acetyl derivative (hexa-acetate ?), apparently identical with that described by Hoffmann and Fari (*loc. cit.*), and a small yield of the same product, accompanied by much amorphous material, was also obtained when rottlerin was boiled with acetic anhydride for 1 hour (compare Perkin and Dutt, *locc. cit.*). All efforts to isolate an acetyl derivative, m. p. 130—135° (Perkin) or m. p. 165° (Dutt), were unsuccessful. In this connexion it may be noted that prolonged treatment of rottlerin with hot formic acid, acetic acid, or acetic anhydride resulted in the formation of amorphous products from which crystalline material could not be obtained. Attempts to methylate rottlerin with methyl sulphate and aqueous sodium hydroxide under a variety of conditions invariably yielded resinous materials, a result which is readily explained by the instability of rottlerin to dilute aqueous sodium hydroxide. On this account also it is clear that the crystalline methylation product described by Dutt (*loc. cit.*) cannot be regarded as a methyl ether of unchanged rottlerin. Less drastic methylating reagents, diazomethane and methyl iodide–potassium carbonate, gave equally unsatisfactory results.

Treatment of rottlerin with phenylhydrazine led to the formation of an amorphous product as recorded by Bartolotti (*loc. cit.*), and similarly intractable products were obtained by the action of semicarbazide acetate and with hydroxylamine hydrochloride.

In the course of a considerable number of experiments on the hydrolytic fission of rottlerin it was found that the nature of the products depends to a large extent on the conditions employed. We have confirmed the formation of rottlerone * along with traces of benzaldehyde when rottlerin is warmed with aqueous sodium carbonate as described by Perkin (*loc. cit.*), but the yield of crystalline material was small and inconsistent. The same products were obtained by means of warm aqueous baryta and thus Telle's ψ-rottlerin (*loc. cit.*) is identical with rottlerone, for which Perkin did not give a melting point. Under both sets of conditions we have found that rottlerone is accompanied by *C*-methylphloroglucinol. On the other hand, with hot concentrated aqueous potassium hydroxide in the absence of zinc dust, rottlerin gave rise to phloroglucinol, acetic acid, benzoic acid, and cinnamic acid (compare Perkin, *loc. cit.*), and with boiling dilute aqueous sodium hydroxide and zinc dust *C*-methyl- and *C*-dimethyl-phloroglucinol together with β-phenylpropionic acid were produced in agreement with the findings of Hermann (*loc. cit.*) and of Telle (*loc. cit.*). Contrary to the results of Telle, however, all attempts to obtain *C*-trimethylphloroglucinol by means of boiling 2% aqueous sodium hydroxide and zinc dust were entirely unsuccessful. Under the latter conditions this author also obtained a small amount of a steam-volatile, camphor-like solid, m. p. 170—172°, but although the crude volatile product isolated by us had a strong camphoraceous odour, the pure solid, m. p. 175°, was odourless; the smell was observed to be due to traces of neutral oily material. For the solid, which reacts with 2 : 4-dinitrophenylhydrazine, the provisional formula $C_{18}H_{18}O$ is suggested, but the quantity of material obtained from several experiments was too small for a detailed investigation.

Oxidation of rottlerin with alkaline potassium permanganate and of rottlerin acetate with the neutral reagent furnished benzoic acid and acetic acid, but contrary to the statement of Dutt (*loc. cit.*) neither phthalic acid nor terephthalic acid could be detected. Similarly, the results obtained by the action of nitric acid on rottlerin were identical with those described by Perkin (*loc. cit.*), but all attempts to isolate nitro-derivatives of phthalic acid or of terephthalic acid by repetition of Dutt and Goswani's experiments (*loc. cit.*)

* It is clear that this compound is not simply an oxidation product of rottlerin as is implied by the name rottlerone, but there is evidence (present work) that the compound contains an active carbonyl group and therefore it is convenient to retain this designation for the present at least.

have so far been unsuccessful. From a series of quantitative oxidation experiments with alkaline potassium permanganate it has been found that for an empirical formula approximating to $C_{33}H_{30}O_9$ rottlerin yields slightly less than one molecular proportion of benzoic acid and therefore it is clear that rottlerin contains one cinnamyl residue and that in degradation experiments where both cinnamic acid and benzoic acid are formed the latter arises by oxidation of the cinnamyl residue and not as the result of the presence of a second phenyl radical in the molecule. In the ozonolysis of rottlerin the cinnamyl radical gives rise to benzaldehyde, which is accompanied by an intractable resin.

On hydrogenation with a palladium catalyst rottlerin gives rise to a tetrahydro-derivative, m. p. 215°, the analytical data for which agree remarkably well with the empirical formula $C_{33}H_{34}O_9$. When a platinum catalyst is employed, hydrogenation proceeds beyond the tetrahydro-stage and both rottlerin and tetrahydrorottlerin yield a product, m. p. 178°, which we have termed *perhydrorottlerin* ($C_{33}H_{40}O_9$?). Hoffmann and Fari (*loc. cit.*) describe a tetrahydro-derivative, m. p. 200—201°, which they consider to be $C_{31}H_{34}O_8$, but which is in all probability a slightly impure form of the product obtained in the present work, since the acetate, m. p. 188°, of the latter, also obtainable directly by the hydrogenation of rottlerin acetate, appears to be identical with the acetate, m. p. 183—185°, described by these authors. In consequence we consider that the evidence is insufficient to warrant the adoption of the empirical formula $C_{31}H_{30}O_8$ which they have deduced for rottlerin from that of their tetrahydro-derivative.

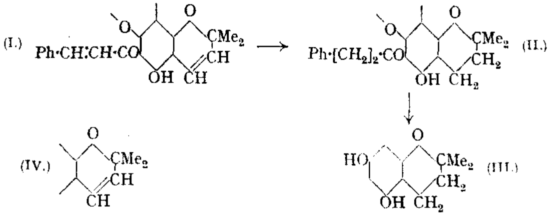
In experiments on the hydrolytic fission of tetrahydrorottlerin with warm dilute aqueous sodium or barium hydroxide a well-crystallised degradation product was formed, which was subsequently found to be identical with *tetrahydrorottlerone* obtained by the hydrogenation of rottlerone with a palladium catalyst. Fission of perhydrorottlerin under similar conditions gave rise to *perhydrorottlerone*, identical with the product formed by the hydrogenation of tetrahydrorottlerone with a platinum catalyst. In the hydrolysis of both tetra- and per-hydrorottlerin the resulting rottlerone derivatives are accompanied by *C*-methylphloroglucinol and a considerable amount of amorphous acidic material.

On account of the extremely poor yields of rottlerone, the purification of which is somewhat difficult, a detailed investigation of this compound is reserved. Since the substance and its hydrogenation products are practically insoluble in aqueous sodium hydroxide but are soluble in an alcoholic solution of this reagent and all give ferric reactions, it is reasonably certain that they contain a phenolic hydroxyl group in the *o*-position to a carbonyl group. The analytical results obtained for rottlerone accord with the formula $C_{20}H_{18}O_4$ or $C_{26}H_{24}O_5$ and for tetrahydrorottlerone with the corresponding formula $C_{20}H_{22}O_4$ (A) or $C_{26}H_{28}O_5$ (B), of which (B) is in closer agreement with the molecular-weight determinations carried out on the tetrahydro-compound and its derivatives. Acetylation and methylation of tetrahydrorottlerone yield an *acetate* and a *methyl ether*, which are both devoid of ferric reactions and are respectively either a diacetate and a dimethyl ether of (A) or a triacetate and a trimethyl ether of (B). Attempts to determine the presence of an active carbonyl group in tetrahydrorottlerone by the usual reagents gave unsatisfactory results, but when the methyl ether was warmed with hydroxylamine hydrochloride in the presence of pyridine a nitrogen-containing product was obtained which appears to be the *oxime*, although the analytical results do not correspond with those required for a derivative of (A) or (B).

Hydrolytic fission of tetrahydrorottlerone with hot concentrated aqueous sodium hydroxide gave rise to β-phenylpropionic acid and a phenolic product which was shown to be 5 : 7-dihydroxy-2 : 2-dimethylchroman (III) by comparison with a synthetical specimen. On the basis of this result it is reasonably certain that tetrahydrorottlerone contains the β-phenylpropionylchroman residue, type (II), a conclusion which is supported by the insolubility of the compound in aqueous sodium hydroxide, its ferric reaction, and the formation of an oxime of its methyl ether.

Further, in view of the fact that the 2 : 2-dimethyl-Δ^3-chromen unit, type (IV), has been shown to be present in the molecular structures of a number of natural compounds (Robertson and co-workers, J., 1933, 489; 1936, 627, 1828; this vol., pp. 279, 286) it is highly probable that rottlerone and rottlerin contain this unit, and, since the residue

appearing as the β-phenylpropionyl radical in the tetrahydro-derivatives has been shown by alkaline hydrolysis and by oxidation to be present as a cinnamyl group in the parent compounds, it is reasonable to suppose that rottlerone and rottlerin contain the cinnamyl-



chromen unit, type (I). The presence of this unit affords a satisfactory explanation of the ease of formation of the tetrahydro-derivatives, because the chromen double bond, like that in the cinnamyl group, has been shown to be readily hydrogenated with a palladium catalyst, *e.g.*, formation of dihydroxanthyletin and dihydroxanthoxyletin (Robertson and co-workers, *loc. cit.*). Further, leaving aside the undetermined part of the molecule, the proved instability of the unit (IV) in toxicarol, xanthoxyletin, and xanthyletin in the presence of alkaline reagents would account to some extent at least for the behaviour of rottlerin on hydrolytic fission.

The conversion of rottlerin and its hydrogenation products into corresponding members of the rottlerone series by means of alkalis under comparatively mild conditions appears to be a complex reaction giving poor yields of crystallisable material, but in each case we have always observed the simultaneous formation of C-methylphloroglucinol. This compound is also obtained along with much resinous material when rottlerin is warmed with dilute hydrochloric acid. These reactions are suggestive that rottlerin may be a depside type of ester, but we have been unable to obtain decisive evidence on this point. The results of the present investigation, however, clearly disprove the structure proposed for rottlerin by Dutt and Goswani (*loc. cit.*).

Experimental.

Rottlerin.—Kamala (250 g.) was heated with boiling benzene (2 l.) for 8 hours, and on being kept for 12 hours the extract, which had been filtered from the yellow insoluble residue (118 g.), deposited part of the rottlerin (11 g.), m. p. 198°. After the isolation of the solid and the evaporation of the greater part of the solvent the residual solution (330 c.c.) gradually deposited more rottlerin (31 g.). As a rule further concentration failed to yield more crystalline material and the resinous residue has been saved for further investigation. The benzene-insoluble material was further extracted with fresh solvent, which was then employed for the extraction of fresh batches of kamala.

Thus obtained, the crude rottlerin was contaminated with considerable quantities of resinous material, and after numerous experiments the following procedure was found to be the most efficacious method of purification : The crude product (600 g.) was boiled with carbon tetrachloride (1·3 l.) for 4 hours, and the solid isolated and extracted with fresh solvent (700 c.c.). The resulting insoluble product (380 g.), m. p. 206°, consisting of fairly pure rottlerin, was purified by repeated crystallisation from ethyl acetate (about 100 g. of solid dissolved in 1·3 l. of solvent), being finally obtained in light reddish-brown plates or needles having a golden lustre (70 g.), m. p. 212°, unchanged by repeated crystallisation from acetone [Found (mean of six analyses) : C, 69·69 (± 0·11); H, 5·57 (± 0·21). Calc. for $C_{33}H_{30}O_9$: C, 69·44; H, 5·30%. Calc. for $C_{31}H_{30}O_8$: C, 70·16; H, 5·7%. Calc. for $C_{34}H_{32}O_9$: C, 69·86; H, 5·48%] (Perkin, Dutt, and Hoffmann and Fari, *locc. cit.*, respectively give m. p. 191—191·5°, 206—207°, 206—207°). Rottlerin is readily soluble in pyridine or aniline, moderately soluble in hot acetone, ethyl acetate, benzene, toluene, chloroform or ether, and sparingly soluble in cold alcohol or acetic acid. It reduces Fehling's solution and gives a reddish-brown coloration with alcoholic ferric chloride.

The mixture obtained by the interaction of rottlerin (3 g.) with acetic anhydride (30 c.c.) and pyridine (15 c.c.) at room temperature for 5 days was poured into ice and acetic acid, and the granular precipitate collected 24 hours later, washed with dilute acetic acid, and recrystallised from acetone–alcohol, giving the acetyl derivative in stout colourless prisms, m. p. 213°, insoluble in aqueous sodium hydroxide and having a negative ferric reaction (Found: C, 66·1; H, 5·3; CH_3·CO, 34·7, 35·8, 38·5%) (Hoffmann and Fari, *loc. cit.*, give m. p. 212°).

Acetylation of rottlerin according to the procedure of Dutt (*loc. cit.*) gave a small yield of the same acetate, m. p. and mixed m. p. 213°, when the reaction mixture was heated for 1 hour, but if the heating was continued for longer periods amorphous products were obtained.

Oxidation of Rottlerin with Alkaline Potassium Permanganate.—1% Aqueous potassium permanganate (approx. 2·5 l.) was slowly added to a solution of rottlerin (10 g., well powdered) in 2% aqueous sodium hydroxide (300 c.c.) until the solution retained a permanganate colour; precautions were taken to prevent the loss of traces of benzaldehyde formed in the early stages of the reaction. The manganese dioxide was removed (wash with hot water), the excess of permanganate destroyed with sulphur dioxide, the solution acidified with dilute sulphuric acid and repeatedly extracted with ether, and the combined dried extracts evaporated, leaving a pale yellow residue (2·2 g.) containing a little acetic acid. Crystallisation of the product, which had been dried in a vacuum at room temperature, from the minimum volume of hot water gave benzoic acid in colourless plates (1·8 g.), m. p. 121° (theoretical for one cinnamyl residue, 2·14 g.); approximately the same yield of benzoic acid was obtained in three experiments. In another experiment the acetic acid was isolated and identified by conversion into the anilide, m. p. 112°.

Action of Aqueous Sodium and Potassium Hydroxide on Rottlerin.—(A) Rottlerin (10 g.) was heated with 50% aqueous potassium hydroxide (50 g.) at 150—160° for ¾ hour in an atmosphere of nitrogen, and the cooled mixture dissolved in water (300 c.c.), acidified with hydrochloric acid, and repeatedly extracted with ether. After the removal of the acidic material from the combined extracts with aqueous sodium bicarbonate evaporation of the solvent left a brown semi-solid, which was extracted once with hot benzene (5 c.c.). A hot aqueous solution of the benzene-insoluble residue was treated with charcoal, filtered, and evaporated in a vacuum at room temperature and the resulting phloroglucinol, which gradually separated in colourless plates (0·1—0·2 g.), m. p. 214—215°, was identified by comparison with an authentic specimen and by conversion into the triacetate, m. p. and mixed m. p. 105—106° (Found: C, 57·2; H, 4·9. Calc. for $C_{12}H_{12}O_6$: C, 57·1; H, 4·8%).

Acidification of the sodium bicarbonate solution gave cinnamic acid (isolated with ether), m. p. and mixed m. p. 133°, after purification.

When a mixture of rottlerin (5 g.) and 50% aqueous potassium hydroxide (50 c.c.) was gradually heated to 250° and kept at this temperature for 10 minutes, cinnamic acid and acetic acid could be isolated in the usual manner.

(B) Well-powdered rottlerin (10 g.) was boiled with 15% aqueous sodium hydroxide (100 c.c.) containing zinc dust (20 g.) for 5 minutes, and the mixture cooled, diluted with water (300 c.c.), and filtered. The filtrate was acidified with sulphuric acid and next day the precipitated resinous solid was removed, the excess of acid neutralised with sodium bicarbonate, and the solution extracted with ether (200 c.c. × 10); the red-brown viscous oil left on evaporation of the solvent was digested with water, and the aqueous soluble fraction isolated by means of ether and boiled with six successive portions of benzene (75 c.c.). In the course of 12 hours the first two benzene extracts deposited crystalline material and in the first case this was further purified by means of warm benzene. The two products, 0·1 g. and 0·15 g., m. p. 150—155°, were then combined and recrystallised from ethyl acetate–xylene, giving *C*-dimethylphloroglucinol in colourless needles, m. p. 162°, identical with an authentic specimen and giving the characteristic blue-violet ferric reaction (Found: C, 62·5; H, 6·5. Calc. for $C_8H_{10}O_3$: C, 62·3; H, 6·5%). On being kept, the remaining benzene extracts deposited resinous material only.

When the brown benzene-insoluble residue was heated in a high vacuum at about 160°, a small amount of sublimate, m. p. 200°, was obtained which on crystallisation from ethyl acetate–xylene gave *C*-methylphloroglucinol (characteristic blue ferric reaction), m. p. 212—213°, identical in every way with an authentic specimen.

(C) A solution of rottlerin (10 g.) in 2% aqueous sodium hydroxide (1·2 l.), containing zinc dust (100 g.), was distilled with the addition of water to keep the volume of the solution approximately constant; from the camphoraceous aqueous distillate, which was collected in the course of 8 hours, a small amount of a crystalline solid separated in colourless needles contaminated

with traces of oily material. Recrystallisation of this solid from light petroleum (b. p. 60—80°) gave colourless, odourless, diamond-shaped plates (25 mg.), m. p. 175°, which reacted with an aqueous-alcoholic solution of 2 : 4-dinitrophenylhydrazine hydrochloride (Found: C, 86·4; H, 7·0. $C_{18}H_{18}O$ requires C, 86·4; H, 7·2%).

A thorough investigation of the phenolic products in the aqueous alkaline liquors from a number of experiments failed to reveal the presence of *C*-trimethylphloroglucinol. The only phenolic compounds isolated were *C*-methyl- and *C*-dimethyl-phloroglucinol.

Tetrahydrorottlerin.—For the preparation of this compound in quantity rottlerin (10 g.), dissolved in ethyl acetate (250 c.c.), was hydrogenated with a palladium-charcoal catalyst (from 0·2 g. of palladium chloride and 2 g. of charcoal); the end of the reaction was indicated when the orange-red solution had become almost colourless. On isolation the product (yield, almost theoretical) separated from alcohol in pale yellow, elongated prisms, m. p. 215° (Found: C, 69·0, 69·0, 68·9; H, 6·0, 6·1, 6·1. Calc. for $C_{31}H_{30}O_8$: C, 69·7; H, 6·4%. Calc. for $C_{33}H_{34}O_9$: C, 69·0; H, 5·9%. Calc. for $C_{34}H_{38}O_9$: C, 69·2; H, 6·4%). The same compound was obtained by means of a palladium-barium sulphate catalyst in acetic acid, ethyl acetate, or acetone and in a series of quantitative experiments at atmospheric pressure it was found that 0·3 g. of rottlerin absorbed approximately 27·4 c.c. of hydrogen; the theoretical quantity for saturation of two double bonds in a compound having a formula approximately $C_{33}H_{30}O_9$ is 23 c.c. Tetrahydro-rottlerin, which is slightly more soluble in organic solvents than rottlerin, forms a yellow solution with aqueous sodium hydroxide and gives an intense green-violet coloration with alcoholic ferric chloride. When a solution of tetrahydrorottlerin (2 g.) in 50% aqueous sodium hydroxide (50 c.c.) was gradually heated to 270°, then kept at this temperature for 15 minutes, cooled, and acidified, β-phenylpropionic acid, m. p. and mixed m. p. 47°, was isolated with ether.

Acetylation of tetrahydrorottlerin (1·5 g.) with acetic anhydride (7·5 c.c.) and pyridine (5 c.c.) at room temperature for 3 days gave the hexa-acetate (2 g.), which separated from methyl alcohol in colourless prisms or plates, m. p. 188°, insoluble in aqueous sodium hydroxide and having a negative ferric reaction [Found: C, 65·5; H, 5·6; $CH_3{\cdot}CO$, 37·34, 36·6. Calc. for $C_{33}H_{28}O_9(CH_3{\cdot}CO)_6$: C, 65·4; H, 5·6; $CH_3{\cdot}CO$, 31·2%]. Hydrogenation of rottlerin acetate (1·5 g.), dissolved in acetone (50 c.c.), with hydrogen (approx. 2·5 mols. absorbed) and a palladium catalyst gave rise to the same tetrahydro-derivative, m. p. and mixed m. p. 188°.

Rottlerone.—When a filtered solution of rottlerin (20 g.) in saturated aqueous barium hydroxide (750 c.c.) was boiled for 10 minutes, traces of benzaldehyde were evolved, much frothing occurred, and an orange product separated which after cooling was isolated, washed, dried, and extracted (Soxhlet) with ether. On being kept, a solution of the resulting deep red extract in chloroform-alcohol deposited garnet-red, pointed prisms (0·8 g.) of rottlerone, m. p. 236° after repeated crystallisation from the same solvent (Found: C, 74·6; H, 5·6. Calc. for $C_{20}H_{18}O_4$: C, 74·5; H, 5·6%. Calc. for $C_{26}H_{24}O_5$: C, 75·0; H, 5·8%). A similar yield of the compound can be obtained by Perkin's method (*loc. cit.*), but in this case the purification of the product is considerably more difficult and the yield is inconsistent. Rottlerone is soluble in warm chloroform, ethyl acetate, carbon tetrachloride, or pyridine, sparingly soluble in acetic acid or ether, and almost insoluble in alcohol, light petroleum, or aqueous sodium hydroxide. On the addition of ferric chloride to an alcoholic solution of the substance a brown coloration slowly develops.

The baryta liquors were acidified with hydrochloric acid, filtered to remove precipitated resinous material, treated with excess of sodium bicarbonate, and extracted with ether (300 c.c. × 10). The product was digested with boiling benzene (50 c.c.) and *C*-methylphloroglucinol, m. p. 209—210°, was isolated from the insoluble residue by sublimation at about 160° in a high vacuum and recrystallised from ethyl acetate-xylene; m. p. and mixed m. p. 214° (Found: C, 60·1; H, 5·8. Calc. for $C_7H_8O_3$: C, 60·0; H, 5·7%). Perkin's method also gave rise to *C*-methylphloroglucinol.

Tetrahydrorottlerone.—(A) On being heated to its boiling point, the yellow solution of tetrahydrorottlerin (1 g.) in 8% aqueous sodium hydroxide (20 c.c.) darkened at about 88—90° and a yellow semi-solid (0·25 g.) separated, which was isolated from the cooled solution with ether and on crystallisation from acetone gave *tetrahydrorottlerone* in slender yellow prisms, m. p. 172—173°, having a violet-green ferric reaction in alcohol [Found (mean of five analyses): C, 74·1; H, 6·7. $C_{20}H_{22}O_4$ requires C, 73·6; H, 6·7%. $C_{26}H_{28}O_5$ requires C, 74·3; H, 6·7%]. The compound is soluble in benzene or chloroform and almost insoluble in aqueous sodium hydroxide. When a solution of tetrahydrorottlerin (5 g.) in saturated aqueous barytra (200 c.c.) was boiled for 5 minutes, a somewhat inferior yield of tetrahydrorottlerone was obtained, m. p. 172—173° after purification.

Acidification of the alkaline liquors left on removal of the tetrahydrorottlerone gave rise to a product, which was isolated with ether and resolved into an amorphous acidic fraction and a small amount of *C*-methylphloroglucinol. The latter compound, m. p. 214°, was separated from accompanying resinous impurities and purified as previously described.

Acetylation of tetrahydrorottlerone (0·5 g.) with acetic anhydride (12 c.c.) and pyridine (5 c.c.) at room temperature for 12 hours and then at 100° for ¾ hour gave the *acetyl* derivative, which formed colourless slender prisms, m. p. 214—215°, from acetone–alcohol (ferric reaction negative) [Found: C, 70·6; H, 6·3; CH_3·CO, 25·3. $C_{26}H_{26}O_4(CO·CH_3)_2$ requires C, 70·2; H, 6·4; CH_3·CO, 21·0%. $C_{26}H_{25}O_5(CO·CH_3)_3$ requires C, 70·3; H, 6·2; CH_3·CO, 23·6%].

(B) Hydrogenation of rottlerone (0·2 g.), dissolved in ethyl acetate (50 c.c.), with a palladium–charcoal catalyst (from 0·1 g. of palladium chloride) was complete in about 3 hours and on isolation the product separated from acetone in yellow prisms, m. p. 172—173°, identical with a specimen obtained by method (A).

Methylation of Tetrahydrorottlerone.—This was effected with the substance (1 g.), methyl iodide (3 c.c.), and potassium carbonate (4 g.) in boiling acetone (100 c.c.) in the course of 8 hours; after 3 hours more iodide (3 c.c.) and carbonate (4 g.) were added. On isolation the *product*, which did not give a ferric reaction, solidified in contact with a little methyl alcohol and then formed colourless prisms, m. p. 102°, from light petroleum (b. p. 60—80°), easily soluble in alcohol or acetone and insoluble in aqueous sodium hydroxide [Found (mean of four analyses): C, 74·9; H, 7·5; OMe, 18·5; *M*, 497, 478. $C_{20}H_{20}O_2(OMe)_2$ requires C, 74·6; H, 7·3; OMe, 17·5%; *M*, 354. $C_{26}H_{25}O_2(OMe)_3$ requires C, 75·3; H, 7·4; OMe, 20·0%; *M*, 462]. This compound was recovered unchanged after being treated with warm acetic anhydride and pyridine.

Treatment of the ether (0·5 g.) with hydroxylamine hydrochloride (0·5 g.) and pyridine (5 c.c.) at 100° for 6—8 hours gave rise to a small yield of a *product*, m. p. 188°, which separated from aqueous alcohol in tiny prisms, m. p. 204—205° (Found: C, 72·1; H, 7·3; N, 4·0. $C_{22}H_{27}O_4N$ requires C, 71·6; H, 7·3; N, 3·8%. $C_{29}H_{35}O_5N$ requires C, 73·0; H, 7·3; N, 2·9%).

Perhydrorottlerin, obtained by hydrogenation of rottlerin (1 g.) in pure acetone (150 c.c.) with hydrogen at 40 lb./sq. in. and a platinum oxide (0·1 g.) catalyst during 48 hours, separated from alcohol in clusters of yellow needles, m. p. 178°. Hydrogenation of tetrahydrorottlerin by this procedure gave the same product, m. p. 178° after purification (Found: C, 68·4; H, 7·3. $C_{33}H_{40}O_9$ requires C, 68·2; H, 7·0%. $C_{34}H_{44}O_9$ requires C, 68·5; H, 7·4%). The properties of this compound are similar to those of tetrahydrorottlerin except that it is slightly more soluble in organic solvents. With alcoholic ferric chloride it gives a violet-green coloration.

Perhydrorottlerone was prepared from the foregoing substance (1 g.) by means of 8% aqueous sodium hydroxide (20 c.c.) according to the procedure used for the preparation of tetrahydrorottlerone; on crystallisation from acetone it formed yellow prisms, m. p. 166°, giving (slowly) a violet-green coloration with alcoholic ferric chloride (Found: C, 73·0; H, 8·3. $C_{20}H_{28}O_4$ requires C, 72·3; H, 8·4%. $C_{26}H_{34}O_5$ requires C, 73·2; H, 8·0%). The same compound, m. p. and mixed m. p. 166°, was obtained by hydrogenation of tetrahydrorottlerone with a platinum catalyst.

Hydrolytic Fission of Tetrahydrorottlerone.—Tetrahydrorottlerone is almost insoluble even at high temperatures in hot aqueous sodium or potassium hydroxide and it was found necessary to use an aqueous alcoholic solution of the reagent in order to obtain a homogeneous solution. The compound (0·6 g.) dissolved readily in a warm mixture of 75% aqueous potassium hydroxide (50 c.c.) and alcohol (25 c.c.) and the resulting pale yellow solution was maintained at 160—170° for ¾ hour in an atmosphere of nitrogen. After cooling, the reaction mixture was acidified with excess of hydrochloric acid, the excess of acid neutralised with sodium bicarbonate, and the solution extracted several times with ether. Sublimation of the residue left on evaporation of the extracts gave colourless prisms (0·23 g.) of 5 : 7-dihydroxy-2 : 2-dimethylchroman, which on recrystallisation from benzene had m. p. 162° and was identical in every way with a synthetical specimen (Bridge, Heyes, and Robertson, this vol., p. 279) (Found: C, 68·1; H, 7·1. Calc. for $C_{11}H_{14}O_3$: C, 68·0; H, 7·2%).

From the aqueous liquor left on removal of the chroman, which had been acidified with hydrochloric acid, only β-phenylpropionic acid, m. p. and mixed m. p. 47°, was isolated with ether.

C-*Methylphloroglucinol.*—This was prepared by the reduction of phloroglucinolaldehyde (1 g.), dissolved in acetic acid (25 c.c.), with hydrogen and a palladium–charcoal catalyst (from 1 g. of charcoal and 5 c.c. of 4% aqueous palladium chloride) in the course of 4 hours and on isolation was purified by sublimation in a high vacuum and then by crystallisation from ethyl

acetate–xylene, forming colourless needles (0·3 g.), m. p. 215—216°, identical with an authentic specimen (Curd and Robertson, J., 1933, 437) (Found: C, 60·1; H, 5·7%).

C-Dimethylphloroglucinol (0·25 g.) was obtained from *C*-methylphloroglucinolaldehyde (0·5 g.) (Herzig and co-workers, *Monatsh.*, 1903, **24**, 876) by the same procedure, m. p. 163° after sublimation and recrystallisation from ethyl acetate–xylene (Found: C, 62·3; H, 6·6%).

The authors thank Mr. A. B. Percival, B.Sc., for assistance with the experiments on the hydrogenation of rottlerin.

UNIVERSITY OF LIVERPOOL. [*Received March 6th*, 1937.]

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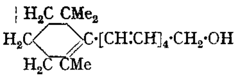
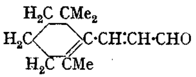
151. *Studies in the Synthesis of Vitamin-A. Part III.*

By J. W. BATTY, A. BURAWOY, I. M. HEILBRON, W. E. JONES, and A. LOWE.

IN Parts I and II (J., 1935, 585; 1936, 561) the preparation of a number of intermediates in the attempted synthesis of vitamin-A has been described, but since one of the main difficulties is the introduction of the side-chain methyl groups in the requisite positions, work has simultaneously been carried out with the object of synthesising ι-(2 : 2 : 6-trimethyl-Δ^{6}-*cyclo*hexenyl)-$\Delta^{\beta\delta\zeta\theta}$-nonatetraen-α-ol (I), which might be expected to resemble the vitamin in physiological properties. The key compound in this proposed synthesis,

(I.) 

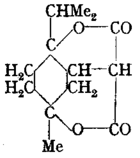
 (II.)

β-(2 : 2 : 6-trimethyl-Δ^{6}-*cyclo*hexenyl)acraldehyde (II) (β-*cyclo*citrylideneacetaldehyde), could theoretically be obtained by direct condensation of acetaldehyde either with β-*cyclo*citral or alternatively with citral and subsequent ring closure of the resultant α-aldehydo-δθ-dimethyl-$\Delta^{\alpha\gamma\eta}$-nonatriene (III) as in the conversion of ψ- into β-ionone. The extension of the side chain would then be effected by further condensation with acetaldehyde or crotonaldehyde Since preliminary experiments on condensations involving β-*cyclo*citral proved unpromising for reasons to be described in a subsequent publication, attention was concentrated on the alternative route.

At the commencement of this work, the only method of preparation of α-aldehydo-δθ-dimethyl-$\Delta^{\alpha\gamma\eta}$-nonatriene (III) described in the literature, apart from a very brief statement concerning its formation by the condensation of citral with acetaldehyde in the presence of sodium hydroxide (Anon., *Chem. Zentr.*, 1932, I, 2104), was the reduction of the phenylimido-chloride of the corresponding acid with chromous chloride (v. Braun and Rudolph, *Ber.*, 1934, **67**, 1735). Since this method did not appear suited to the preparation of relatively large quantities of the aldehyde, an alternative route was investigated.

$CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CMe{:}CH{\cdot}CH{:}CH{\cdot}CHO$
(III.)

$CMe_2{:}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CMe{:}CH{\cdot}CH{:}C(CO_2H)_2$
(IV.)

 (V.)

By the condensation of citral with malonic acid in the presence of pyridine, Verley (*Bull. Soc. chim.*, 1899, **21**, 415) obtained a mixture of δθ-dimethyl-$\Delta^{\alpha\gamma\eta}$-nonatriene-α-carboxylic acid and a solid which he assumed to be citrylidenemalonic acid. A detailed investigation of the latter compound, however, by Kuhn and Hoffer (*Ber.*, 1931, **64**, 1243) led these authors to the conclusion that it did not possess the structure (IV) but was more probably a cyclic dilactone (V).

In support of the view that (IV) cannot represent the true structure, we have found that, whereas such a substance would be expected to exhibit selective absorption in the region of 3000 A., the compound in question shows only general absorption and moreover fails to give acetone on treatment with ozonised oxygen. This anomalous behaviour appears to be limited to the compound under discussion, since the citrylidenecyanoacetic acid, m. p. 122°, of Tiemann (*Ber.*, 1898, **31**, 3329) exhibits a well-defined band at 3005 A. (Table II) and, in contrast to "citrylidenemalonic acid," is readily soluble in cold dilute sodium hydroxide solution. We have further ascertained that "citrylidenemalonic acid" is decarboxylated quantitatively on distillation under reduced pressure in presence of a trace of copper-bronze, giving δθ-dimethyl-$\Delta^{\alpha\gamma\eta}$-nonatriene-α-carboxylic acid, b. p. 125—130°/1 mm. (*methyl* ester, b. p. 137—140°/15 mm.), the facile formation of which is difficult to reconcile with formula (V).

Distillation of the barium salt of the monocarboxylic acid with barium formate under reduced pressure gives α-aldehydo-δθ-dimethyl-$\Delta^{\alpha\gamma\eta}$-nonatriene (III) in 30% yield, which shows a well-defined absorption band at 2900 A. (Table II), a position in good agreement with theoretical deductions. Contrary, however, to the observation of v. Braun and Rudolph (*loc. cit.*), who record two semicarbazones, m. p. 150° and 93—102°, we could only obtain one semicarbazone, m. p. 167°, in agreement with the findings of Kuhn, Badstübner, and Grundmann (*Ber.*, 1936, **69**, 104), who, while this work was in progress, published details of the preparation of (III) by condensation of citral with acetaldehyde in the presence of a piperidine–acetic acid catalyst. We have repeated the preparation of (III) according to the latter authors' method and find that both the aldehyde and its semicarbazone ($\lambda_{max.}$ 3045 A.; Table II) are spectroscopically identical with those obtained by the alternative method; further, no depression in m. p. was observed on admixture of the two semicarbazones.

α-Aldehydo-δθ-dimethyl-$\Delta^{\alpha\gamma\eta}$-nonatriene condenses readily with cyanoacetic acid in the presence of aqueous alkali, giving *α-cyano-ζχ-dimethyl-$\Delta^{\alpha\gamma\epsilon\iota}$-undecatetraene-α-carboxylic acid* (VI) as a viscous oil which, like citrylidenecyanoacetic acid (cf. Tiemann, *loc. cit.*), presumably consists of a mixture of isomers. Repeated extraction of the oil with light petroleum gave a crystalline solid, m. p. 150° ($\lambda_{max.}$ 3480 A.; Table II), which appeared to be a single modification of (VI); the remainder of the oil could not be obtained solid.

(VI.) $R\cdot CMe{:}CH\cdot CH{:}CH\cdot CH{:}C(CN)\cdot CO_2H$ $\qquad$ $R\cdot C{<}\begin{array}{l}CH\cdot CHO\\ CH{:}CH\cdot CH{:}CH\cdot CH_3\end{array}$ (VII.)

(VIII.) $R\cdot CMe{:}CH\cdot[CH{:}CH]_2\cdot CHO$ $\qquad$ $R\cdot C{<}\begin{array}{l}CH\cdot CH{:}CH\cdot CHO\\ CH{:}CH\cdot CH_3\end{array}$ (IX.)

($R = CMe_2{:}CH\cdot CH_2\cdot CH_2$.)

An examination of the mother-liquors from which the semicarbazone of (III), prepared by the method of Kuhn, Badstübner, and Grundmann (*loc. cit.*), had been isolated revealed the presence of a small quantity of a second *semicarbazone*, m. p. 158°. Analysis of this proved it to be derived from a condensation product of citral with two molecules of acetaldehyde and, on the assumption that it is an alicyclic compound, the fact that it shows a well-defined absorption band at 3255 A. (Table II) indicates the presence of a conjugated system of the type $>C{=}C{-}C{=}C{-}C{=}C{-}C{=}O$. On this evidence the parent aldehyde might be either (VII), (VIII), or (IX). In order to gain further information regarding this product, and also to explore the possibility of obtaining (VIII) directly, we have made a detailed study of the condensation of citral with crotonaldehyde, employing the piperidine–acetic acid catalyst. The general method of working up the complex reaction mixture is summarised in Table I, but so far only fractions A, B, and C have been examined in detail.

Fraction A.—Refractionation of this gave a main portion, b. p. 86—88°/0·03 mm. (36 g.), yielding a *semicarbazone*, m. p. 206°. This showed an absorption band at 3255 A. (Table II), from which it follows that it contains the same conjugated system as the semicarbazone, m. p. 158°, referred to above, with which, as shown by analysis, it is isomeric.

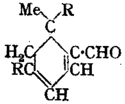
TABLE I.

Citral (1500 g.) + crotonaldehyde (3600 g.)

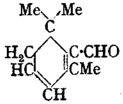
- Crude condensation product
  - Fractionated at 30 mm.
    - Water + crotonaldehyde
    - Citral (600 g.)
    - Residue
      - Distilled up to 200°/30 mm. (Claisen flask)
        - Distillate
          - Fractionated (Widmer column)
            - Citral (400 g.)
            - Fraction A (56 g.) B. p. 95—105°/0·1 mm.
              - Refractionated: B. p. 97—101°/0·1 mm. or 86—88°/0·03 mm. (36 g.)
                - Semicarbazone, m. p. 206°
            - Fraction B (210 g.) B. p. 113—120°/0·1 mm.
              - Refractionated: B. p. 115—118°/0·1 mm. (192 g.)
                - Semicarbazone, m. p. 160°
            - Fraction C (48 g.) B. p. 134—138°/0·2 mm.
              - B. p. 126—150°/0·1 mm. (30 g.)
                - Semicarbazone, m. p. 197°
            - Fraction D (15 g.) B. p. 142—145°/0·2 mm.
            - Residue
        - Residue

Fraction B.—Redistillation gave as main fraction (192 g.) a pale yellow oil, b. p. 115—118°/0·1 mm., from which a crude semicarbazone was obtained which on fractional crystallisation yielded a further small quantity of the compound, m. p. 206°. The main product consisted of a *semicarbazone*, m. p. 160°, spectroscopically identical with (Table II), and showing no depression in m. p. on admixture with, the semicarbazone, m. p. 158°, already referred to. The identity of these two compounds eliminates (IX) from further consideration.

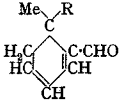
In any discussion of the structures of the aldehydes produced in this condensation, it is necessary to consider, in addition to the various open-chain types, the possibility of the formation of cyclic products. Bernhauer and Irrgang (*Annalen*, 1936, **525**, 43), from preliminary work on the condensation of citral with crotonaldehyde in the presence of baryta, and by analogy with their work on the intermolecular condensation of crotonaldehyde, concluded that their product probably possessed a cyclic structure. Further, Fischer and Löwenberg (*Annalen*, 1932, **494**, 278) have demonstrated that the action of sodamide on citral gives a good yield of a cyclic aldehyde for which structure (X) was tentatively advanced.



(X.)



(XI.)



(XII.)

That, however, the semicarbazone, m. p. 160°, is actually derived from an open-chain aldehyde was evidenced by quantitative microhydrogenation, which revealed the presence of five double bonds, including the semicarbazido-linkage. The further fact that the free *aldehyde*, $C_{14}H_{20}O$ (2 : 4-*dinitrophenylhydrazone*, m. p. 104—105°), regenerated from the semicarbazone by distillation with steam in presence of oxalic acid, has an absorption band at 3140 A. confirms the presence of the conjugated system observed in the case of the semicarbazone (cf. α-aldehydo-$\Delta^{\alpha\gamma\epsilon}$-heptatriene; Hausser, Kuhn, Smakula, and

Hoffer, *Z. physikal. Chem.*, 1935, **29**, 372). In order to differentiate between (VII) and (VIII) the aldehyde was treated with ozone: acetone and lævulaldehyde (isolated as its 2 : 4-dinitrophenylhydrazone) were obtained, a result proving that it is α-aldehydo-ζχ-dimethyl-$\Delta^{\alpha\gamma\epsilon\iota}$-undecatetraene (VIII).

The nature of the difference between the semicarbazones of m. p. 160° and 206° has yet to be determined, but that they are closely related is indicated by their absorption spectra, which, except for a slight difference in the extinction coefficients (Table II), are practically identical. This close similarity is also observed in the *phenylsemicarbazones*, m. p. 173° and 134°, which were obtained by heating the respective semicarbazones, m. p. 206° and 160°, with aniline.

Fraction C.—Redistillation gave a main fraction, b. p. 126—130°/0·1 mm. (30 g.), from which a *semicarbazone*, m. p. 197°, was obtained, which, although isomeric with those from fractions A and B, differs in possessing an absorption band at 2855 A. (Table II), indicating possibly a cyclic structure. That it does not possess structure (XII), however, would appear probable, since such a compound might be expected to show a close spectroscopic similarity to safranal (XI), the semicarbazone of which possesses a band at 3230 A. (Kuhn and Wendt, *Ber.*, 1936, **69**, 1550). Further work is at present in hand with the object of determining the structure of this aldehyde.

As mentioned elsewhere (Heilbron and Jones, *J. Soc. Chem. Ind.*, 1936, **55**, 813), a satisfactory method of converting α-aldehydo-ζχ-dimethyl-$\Delta^{\alpha\gamma\epsilon\iota}$-undecatetraene (VIII) into α-aldehydo-δ-(2 : 2 : 6-trimethyl-Δ^6-*cyclo*hexenyl)butadiene has been worked out and will be reported upon in the near future. The analogous condensation of citral with β-methylcrotonaldehyde is at present being investigated.

TABLE II.

	Compound.	B. p. or M. p.	$\lambda_{max.}$, A.	$\epsilon_{max.}$	Remarks.
(i)	R·CMe:CH·CH:CH·CO_2H	B. p. 132—134°/1 mm.	2720	12,800	From "citrylidenemalonic acid"
(ii)	R·CMe:CH·CH:CH·CHO	B. p. 105—108°/0·1 mm.	2900	15,960	From citral + acetaldehyde
(iii)	Semicarbazone of (ii)	M. p. 166—168°	3045	47,200	From citral + acetaldehyde
(iv)	,, ,, (ii)	M. p. 167°	3045	47,500	From distillation of barium salt of (i)
(v)	R·CMe:CH·[CH:CH]$_2$·CHO	B. p. 114—118°/0·05 mm.	3140	12,490	Regenerated from semicarbazone, m.p. 160°
(vi)	Semicarbazone of (v)	M. p. 158°	3255	28,000	Isolated from mother-liquors of (iii)
(vii)	,, ,, (v)	M. p. 160°	3255	27,100	From citral + crotonaldehyde
(viii)	Phenylsemicarbazone of (v)	M. p. 134°	3320	28,700	From (vii) + aniline
(ix)	Semicarbazone of fraction A	M. p. 206°	3255	24,400	—
(x)	Phenylsemicarbazone of fraction A	M. p. 173°	3320	26,600	From (ix) + aniline
(xi)	Semicarbazone of fraction C	M. p. 197°	2855	21,100	—
(xii)	Anil of (v)	B. p. 178—182°/15 mm.	2680	10,000	—
(xiii)	R·CMe:CH·CH:C(CN)·CO_2H	M. p. 122°	3005	23,100	From citral + cyanoacetic acid
(xiv)	R·CMe:CH·CH:CH·CH:C(CN)·CO_2H	M. p. 150°	3480	34,100	From (ii) + cyanoacetic acid

Solvent, alcohol. R = CMe_2:CH·CH_2·CH_2.

EXPERIMENTAL.

δθ-Dimethyl-$\Delta^{\alpha\gamma\eta}$-nonatriene-α-carboxylic Acid.—"Citrylidenemalonic acid" (35 g., m. p. 186°), prepared as described by Verley (*loc. cit.*) and freed completely from ether-soluble products, was heated with copper-bronze (0·1 g.) at 130—140° (oil-bath temperature) for 1½ hours at 10—15 mm. The liquid residue was then distilled with a free flame, yielding a colourless oil, b. p. 130—135°/1 mm., which on redistillation gave the pure monocarboxylic acid (25 g.), b. p. 132—134°/1 mm.

Methyl δθ-Dimethyl-$\Delta^{\alpha\gamma\eta}$-nonatriene-α-carboxylate.—A solution of the above acid (50 g.) in aqueous sodium bicarbonate (23 g. in 500 c.c. of water) was shaken with methyl sulphate

(17 g.) for 24 hours at room temperature. The suspension was then ether-extracted, and the ethereal solution, after repeated washing with sodium carbonate solution, dried over sodium sulphate. The oil obtained after removal of solvent gave on distillation a main fraction (32 g.), b. p. 137—160°/12 mm., which on redistillation yielded the pure *methyl* ester as a pale yellow oil, b. p. 137—140°/15 mm. (Found : C, 75·2; H, 9·7. $C_{13}H_{20}O_2$ requires C, 75·0; H, 9·6%).

α-Aldehydo-δθ-dimethyl-$\Delta^{\alpha\gamma\eta}$-nonatriene (III).—Redistilled δθ-dimethyl-$\Delta^{\alpha\gamma\eta}$-nonatriene-α-carboxylic acid (24 g.) was dissolved in aqueous potassium hydroxide (7 g. in 60 c.c. of water) and a solution of barium chloride (15 g. in 70 c.c. of water) was slowly added with stirring. The precipitated barium salt, after being dried by suspension in benzene and distillation of the latter under reduced pressure, was thoroughly mixed with anhydrous barium formate (20 g.), and the whole diluted with an equal bulk of silver sand. After being maintained at 150—160°/1 mm. for 1 hour, the mixture was heated directly with a luminous flame until no more liquid distilled. The crude aldehyde (5·5 g.) on redistillation gave pure α-aldehydo-δθ-dimethyl-$\Delta^{\alpha\gamma\eta}$-nonatriene, b. p. 105—110°/0·1 mm. Its semicarbazone crystallised from methyl alcohol in short colourless needles, m. p. 167°, alone or mixed with a specimen, m. p. 166—168°, prepared by the method of Kuhn, Badstübner, and Grundmann (*loc. cit.*).

Condensation of Citral with Acetaldehyde.—Citral (76 g.) was condensed with acetaldehyde exactly as described by Kuhn, Badstübner, and Grundmann (*loc. cit.*), giving α-aldehydo-δθ-dimethyl-$\Delta^{\alpha\gamma\eta}$-nonatriene (14 g.) as a pale yellow oil, b. p. 125—135°/2 mm. The aldehyde (5 g.) was converted into its semicarbazone in the normal manner with alcoholic semicarbazide acetate, and the product fractionally crystallised. In confirmation of the results of Kuhn, Badstübner, and Grundmann, only one semicarbazone, m. p. 166—168°, of α-aldehydo-δθ-dimethyl-$\Delta^{\alpha\gamma\eta}$-nonatriene could be isolated. From the mother-liquors of the above semicarbazone, however, a small quantity of a *semicarbazone* of α-aldehydo-ζχ-dimethyl-$\Delta^{\alpha\gamma\epsilon\iota}$-undecatetraene was isolated by concentration. It crystallised from aqueous methyl alcohol in short colourless needles, m. p. 158° (Found : C, 69·1; H, 8·6; N, 16·0. $C_{15}H_{23}ON_3$ requires C, 69·0; H, 8·8; N, 16·1%).

For spectroscopic examination α-aldehydo-δθ-dimethyl-$\Delta^{\alpha\gamma\eta}$-nonatriene was regenerated from its semicarbazone by distillation in steam with 10% aqueous oxalic acid. It formed a pale yellow oil with an ester-like odour, b. p. 105—108°/0·1 mm.

Condensation of Citral with Crotonaldehyde.—A mixture of citral (250 g.) and crotonaldehyde (100 g.) containing a piperidine–acetic acid catalyst (10 g. of an equimolecular mixture of piperidine and glacial acetic acid in the minimum volume of absolute alcohol) was maintained at 110—120° (oil-bath temperature) in an atmosphere of carbon dioxide. When the internal temperature had reached 100—105°, a further quantity of crotonaldehyde (100 g.) was added : the procedure was repeated until a total of 600 g. of crotonaldehyde had been introduced; the reaction mixture was then maintained at 120° for 1 hour after the last addition of crotonaldehyde. The combined crude condensation product from six runs (1500 g. of citral), after removal of the aqueous layer, was fractionated at 30 mm., a Lapworth column being used to remove water, crotonaldehyde and citral. The residue was distilled from a Claisen flask, the whole of the material which distilled up to 200°/30 mm.being collected and fractionated through a Widmer column. The distillate was separated into the following fractions : (1) citral; (2) fraction A, b. p. 95—105°/0·1 mm.; (3) fraction B, b. p. 113—120°/0·1 mm. (210 g.); (4) fraction C, b. p. 134—138°/0·2 mm. (48 g.); (5) fraction D, b. p. 142—145°/0·2 mm. (15 g.).

Fraction A. After refractionation (Widmer column) this gave a pale yellow oil (36 g.), b. p. 86—88°/0·03 mm., which was treated with alcoholic semicarbazide acetate in the normal manner. The *semicarbazone* crystallised from methyl alcohol, in which it was sparingly soluble in the cold, in colourless needles, m. p. 206°, which slowly turned pale yellow in light (Found : C, 68·9; H, 8·8; N, 16·2. $C_{15}H_{23}ON_3$ requires C, 69·0; H, 8·8; N, 16·1%). For further characterisation the semicarbazone (1 g.) was heated for 15 minutes at 160—180° with aniline (2 g.). The residue was cooled, dissolved in 10% aqueous acetic acid, and extracted several times with ether, the ethereal solution then being washed successively with 10% acetic acid, sodium carbonate solution, and water. After drying over sodium sulphate and removal of the solvent, the residue was repeatedly crystallised from methyl alcohol, giving the corresponding *phenylsemicarbazone* in fine yellow needles, m. p. 173° (Found : C, 74·8; H, 8·1; N, 12·5. $C_{21}H_{27}ON_3$ requires C, 74·8; H, 8·0; N, 12·5%).

Fraction B. Refractionation (Widmer column) gave a main fraction (192 g.), b. p. 115—118°/0·1 mm., which was treated with semicarbazide acetate. Fractional crystallisation from methyl alcohol gave a small quantity of the above semicarbazone, m. p. 206°, and a more soluble isomeric *semicarbazone* crystallising from methyl alcohol in colourless needles, m. p.

160°, which also turned pale yellow on exposure to light (Found: C, 69·0; H, 8·8; N, 16·2. $C_{15}H_{23}ON_3$ requires C, 69·0; H, 8·8; N, 16·1%).

Quantitative microhydrogenation of the semicarbazone, m. p. 160°, by the method of Jackson and Jones (J., 1936, 895) gave the following results: 3·870 mg. of semicarbazone required 1·450 c.c. of hydrogen at 767·5 mm. and 16° (4·1 |=) in the cold, 1·650 c.c. (4·9 |=) on warming (solvent decalin).

The free *aldehyde* of fraction B, obtained by steam-distillation of the semicarbazone, m. p. 160°, with 10% aqueous oxalic acid, was a pale yellow oil, b. p. 114—118°/0·05 mm. (Found: C, 82·6; H, 9·8. $C_{14}H_{20}O$ requires C, 82·4; H, 9·8%). Its *phenylsemicarbazone*, prepared as described above, crystallised from methyl alcohol in yellow needles, m. p. 134° (Found: C, 74·9; H, 8·0; N, 12·3. $C_{21}H_{27}ON_3$ requires C, 74·8; H, 8·0; N, 12·5%). The aldehyde readily formed a 2 : 4-*dinitrophenylhydrazone* by heating with the reagent for a short time in glacial acetic acid, the product crystallising from dilute acetic acid in red micro-needles, m. p. 104—105° (Found: C, 62·6; H, 6·4; N, 14·8. $C_{20}H_{24}O_4N_4$ requires C, 62·5; H, 6·3; N, 14·6%). The *anil* was obtained by heating the aldehyde (10 g.) with aniline (4·5 g.) at 100° for 2 hours; the mixture was then cooled and ether-extracted, the solution dried over sodium sulphate, and the solvent removed. Distillation of the residue gave a main fraction, b. p. 225—230°/25 mm., which on refractionation gave the pure anil as a yellowish-brown viscous oil, b. p. 178—182°/15 mm. (Found: C, 85·7; H, 8·9; N, 4·8. $C_{20}H_{25}N$ requires C, 86·0; H, 9·0; N, 5·0%).

Ozonisation of α-Aldehydo-ζχ-dimethyl-$\Delta^{\alpha\gamma\epsilon\iota}$-undecatetraene.—Ozonised oxygen was passed through a solution of the aldehyde (2 g., regenerated from the semicarbazone, m. p. 160°) in carbon tetrachloride (30 c.c.) for 12 hours. The dark-coloured semi-solid ozonide obtained on removal of solvent by decantation was decomposed by refluxing with water for 1 hour, and the resultant clear solution steam-distilled. The first runnings contained acetone (2 : 4-dinitrophenylhydrazone, m. p. 128°) and the later distillate contained a product which reduced Fehling's solution and gave a yellow, sparingly soluble 2 : 4-dinitrophenylhydrazone. Crystallisation of the latter from nitrobenzene–alcohol gave yellow needles, m. p. 235—236°, which were identified as lævulaldehyde-2 : 4-dinitrophenylhydrazone (Strain, *J. Amer. Chem. Soc.*, 1935, 57, 760) by comparison with an authentic specimen prepared by ozonisation of citral.

Fraction C. The *semicarbazone* from this fraction separated from methyl alcohol as a colourless microcrystalline powder, m. p. 197°, which, in contrast to the semicarbazones from fractions A and B, showed no tendency to turn yellow in light (Found: C, 68·8; H, 8·8; N, 16·0. $C_{15}H_{23}ON_3$ requires C, 69·0; H, 8·8; N, 16·1%).

α-Cyano-ζχ-dimethyl-$\Delta^{\alpha\gamma\epsilon\iota}$-undecatetraene-α-carboxylic Acid (VI).—α-Aldehydo-δθ-dimethyl-$\Delta^{\alpha\gamma\eta}$-nonatriene (5 g.) was shaken with a solution of cyanoacetic acid (4·5 g.) in aqueous sodium hydroxide (2 g. in 100 c.c.) until all the oil had disappeared (about ½ hour). After two extractions with ether, the aqueous suspension of the sodium salt of (VI) was acidified with dilute hydrochloric acid and ether-extracted. Removal of the solvent from the dried ethereal solution left a brown oil (5·5 g.), from which boiling ligroin (b. p. 80—100°) extracted a yellow solid. Repeated crystallisation of the latter from aqueous alcohol yielded one form of *α-cyano-ζχ-dimethyl-$\Delta^{\alpha\gamma\epsilon\iota}$-undecatetraene-α-carboxylic acid* (VI) as a pale yellow, microcrystalline solid, m. p. 150° (Found: C, 73·5; H, 8·0; N, 5·7. $C_{15}H_{19}O_2N$ requires C, 73·5; H, 7·8; N, 5·7%). All attempts to obtain the ligroin-insoluble portion of the condensation product solid have been unsuccessful.

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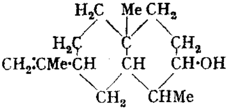
THE UNIVERSITY, MANCHESTER. [*Received, March 8th, 1937.*]

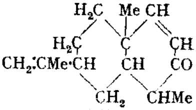
152. *The Constitution of α-Cyperone.*

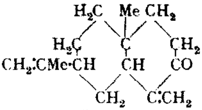
By A. E. BRADFIELD, R. R. PRITCHARD and J. L. SIMONSEN.

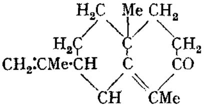
IT was shown by Bradfield, Hegde, Rao, Simonsen, and Gillam (J., 1936, 667) that dihydro-α-cyperol, obtained by the sodium and alcohol reduction of α-cyperone, had the constitution (I). This allows of three alternative structures (II), (III) and (IV) for the parent ketone, and on the evidence then available, the formula (II) was adopted as the most probable.

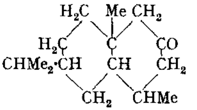
The further study of the apparently anomalous formation of hydroxymethylene-α-cyperone (*loc. cit.*, p. 669) has necessitated a revision of the previous conclusions.


(I.)


(II.)


(III.)

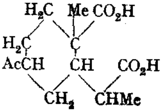
(IV.)


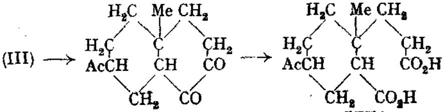

(V.)

By reduction of the hydroxymethylene derivative, followed by dehydrogenation with selenium, a hydrocarbon yielding a picrate, m. p. 102·5—104°, and a *s*-trinitrobenzene derivative, m. p. 116—118°, was obtained. This was not identical with the dimethyl*iso*propylnaphthalene (picrate, m. p. 113—114·5°; *s*-trinitrobenzene derivative, m. p. 141—142°) obtained by dehydrogenation of the product of the action of methylmagnesium iodide on tetrahydroeremophilone. On the basis of the structure (V) assigned to tetrahydroeremophilone by Bradfield, Penfold, and Simonsen (J., 1932, 2744) the latter hydrocarbon was regarded as 1 : 3-dimethyl-7-*iso*propylnaphthalene. The non-identity of the two hydrocarbons was regarded as evidence against the normal formation of a hydroxymethylene derivative and appeared to supply a convincing reason for rejecting (III) and (IV) as representations of α-cyperone, since in both of these there is a methylene group in the 3-position adjacent to the carbonyl group.

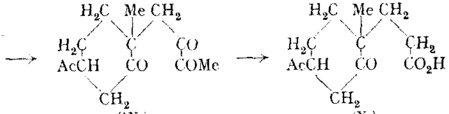
1 : 3-Dimethyl-7-*iso*propylnaphthalene has now been synthesised. Cuminaldehyde was condensed with ethyl α-bromopropionate in the presence of sodium ethoxide, and hydrolysis of the resulting *ester* yielded *cuminyl methyl ketone*. Condensation of this ketone with ethyl bromoacetate, followed by replacement of the hydroxyl group by hydrogen by the usual series of reactions, yielded *ethyl β-cuminylbutyrate*, which was cyclised by treatment with sulphuric acid. Treatment of the tetralone with methylmagnesium iodide and dehydrogenation of the product with selenium yielded 1 : 3-dimethyl-7-*iso*propylnaphthalene, the *picrate* and the *s-trinitrobenzene* derivative of which were identical with the corresponding derivatives of the hydrocarbon obtained from the hydroxymethylene-α-cyperone. In consequence, there is now no reason to suppose that the formation of the hydroxymethylene compound has proceeded abnormally and its formation may therefore be taken as a proof that the carbon atom 3 in α-cyperone carries two hydrogen atoms and as providing a cogent argument for the rejection of (II) and for the retention of either (III) or (IV) as the representation of this ketone.

It follows that the interpretation of the oxidative degradation of the ketone requires reconsideration. Ozonolysis of α-cyperone gave formaldehyde and a liquid ketonic acid, to which, on the basis of the analysis of its liquid methyl ester and of the crystalline semicarbazone of the ester, was ascribed the formula $C_{13}H_{20}O_5$ (VI). An acid of the same composition, but of different structure, could, however, be obtained from the ketone (III) by the further oxidation of the primary product (VII) to (VIII) by the hydrogen peroxide formed during the decomposition of the ozonide. On the other


(VI.)

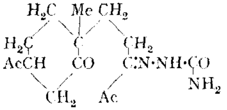

(VII.) (VIII.)

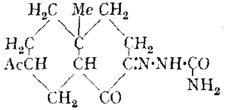
hand, ozonolysis of (IV) would lead to the formation of (IX) as a primary, and the diketonic acid $C_{12}H_{18}O_4$ (X) as a secondary product. The analytical figures previously given (ester: C, 64·3; H, 8·4%; semicarbazone: C, 56·8; H, 7·9%) do not provide a distinction between (VIII) and (X) ($C_{15}H_{24}O_5$ requires C, 63·4; H, 8·5%. $C_{13}H_{20}O_4$ requires C, 65·0; H, 8·3%. $C_{16}H_{27}O_5N_3$ requires C, 56·4; H, 7·9%. $C_{14}H_{23}O_4N_3$ requires C, 56·6; H, 7·7%). Unfortunately a nitrogen determination which would have distinguished the two semicarbazones was not made.

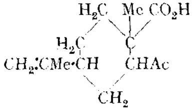
(IV) 

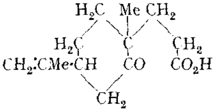
(IX.) (X.)

We must turn therefore to the product of the ozonolysis of α-cyperone semicarbazone, for which analysis requires the composition $C_{15}H_{23}O_4N_3$, to differentiate between (III) and (IV). This we now regard as having the structure (XI), derived from (IV), since the product (XII) which would be expected from (III) has the composition $C_{14}H_{21}O_3N_3$.

(XI.) 

 (XII.)

(XIII.) 

 (XIV.)

It was mentioned (*loc. cit.*, p. 668) that by the action of hydrogen peroxide in alkaline solution on α-cyperone a small yield of a ketonic acid, $C_{13}H_{20}O_3$, was obtained, which, on the basis of (II), was considered to be 6-acetyl-1-methyl-4-*iso*propenyl*cyclo*hexane-1-carboxylic acid (XIII). On the basis of (IV) this acid must now be represented as 1-methyl-4-*iso*propenyl*cyclo*hexan-2-one-1-propionic acid (XIV). It is difficult to derive a keto-acid of the required composition from the alternative formula (III).

In view of the considerations now advanced, we conclude, therefore, that (IV) is the most satisfactory representation of α-cyperone and since β-cyperone semicarbazone gives the same degradation product as α-cyperone semicarbazone, the two ketones must presumably be stereoisomerides, differing in the disposition of the angle methyl and the *iso*propenyl group. It is somewhat remarkable that the interchange between the two forms should take place with such facility.

In advancing this structure for α-cyperone we desire to emphasise the fact that our conclusions are based ultimately on the dehydrogenation of dihydro-α-cyperol to eudalene and on the assumption of an angle methyl group in position 9. We are at present engaged, in collaboration with Professor R. Robinson, in attempting the synthesis of the ketone.

The fact that the product from the action of methylmagnesium iodide on tetrahydroeremophilone does not, on dehydrogenation, yield 1 : 3-dimethyl-7-*iso*propylnaphthalene throws doubt on the structures assigned to eremophilone and its congeners. The constitution of these ketones will be discussed in a future communication.

EXPERIMENTAL.

Ethyl αβ-Epoxy-β-cumyl-α-methylpropionate.—In the course of 3 hours, powdered sodium ethoxide (47 g.) was added, with occasional shaking, to a mixture of cuminaldehyde (100 g.) and ethyl α-bromopropionate (122 g.), cooled in a freezing mixture. After standing overnight, the

mixture was warmed on the water-bath for 6 hours. After the addition of ice-water and dilute acetic acid, the product was extracted with ether, the extract washed with water and dried, and the ether removed, leaving an oil, which was twice fractionated. The *ester* (66 g.) boiled at 180—181°/24 mm. (Found : C, 72·4; H, 8·1. $C_{15}H_{20}O_3$ requires C, 72·6; H, 8·1%).

Cuminyl Methyl Ketone.—The above ester (66 g.) was refluxed with methyl-alcoholic potassium hydroxide (potassium hydroxide, 30 g.) for 3 hours. After addition of water and removal of the alcohol by distillation, the solution was acidified and extracted with ether. The acid remaining after evaporation of the ether was heated at 180° for 5 hours. The product was submitted to steam distillation, the ketone passing over, and a brown residue (A) being left in the flask. The ketone was collected in ether, and the extract washed with sodium carbonate solution, removing some cuminic acid, dried, and evaporated. The *ketone* distilled at 137°/22 mm. (Found : C, 81·4; H, 9·0. $C_{12}H_{16}O$ requires C, 81·8; H, 9·1%). The *semicarbazone* crystallised from methyl alcohol in rosettes of prismatic needles, m. p. 142—143° (Found : N, 17·7. $C_{13}H_{19}ON_3$ requires N, 18·0%). The 2 : 4-*dinitrophenylhydrazone* crystallised from alcohol, in which it was very sparingly soluble, in golden leaflets, m. p. 137—138° (Found : N, 15·5. $C_{18}H_{20}O_4N_4$ requires N, 15·7%). The residue (A) crystallised from chloroform, in which it was sparingly soluble, in fine needles, decomp. 170—171°, and was undoubtedly αβ-*dihydroxy-β-cumyl-α-methylpropionic acid* (Found : C, 65·4; H, 7·8. $C_{13}H_{18}O_4$ requires C, 65·5; H, 7·6%).

Ethyl β-Cuminylbutyrate.—A mixture of cuminyl methyl ketone (26 g.), ethyl bromoacetate (22 g.), and zinc (9·7 g.) in dry benzene (250 c.c.) was heated on the water-bath, reaction initiated by the addition of a little methylmagnesium iodide, and the heating continued for 3 hours. The cooled solution was shaken with dilute sulphuric acid until the benzene layer became clear, ether added, and the ethereal solution separated and washed with dilute sulphuric acid, potassium carbonate solution, and water, dried, and evaporated. The residue was fractionated under reduced pressure. The fraction (25·2 g.), b. p. 160—200°/16 mm., which consisted of a mixture of unsaturated ester and hydroxy-compound, was heated with an equal weight of potassium hydrogen sulphate for 8 hours, and the product without further purification was reduced in ethyl-alcoholic solution by hydrogen in the presence of palladium–norit catalyst, yielding the *butyrate*, b. p. 170—174°/18 mm. (Found : C, 78·0; H, 9·7. $C_{16}H_{24}O_2$ requires C, 77·4; H, 9·7%).

3-*Methyl*-7-iso*propyl*-1 : 2 : 3 : 4-*tetral*-1-*one.*—The above ester (18·2 g.) was heated on the water-bath with a mixture of sulphuric acid (135 c.c.) and water (45 c.c.) for 1¼ hours. The cooled solution was poured into water, and the product extracted with ether. The residue after evaporation of the ether was refluxed with alcoholic potassium hydroxide (potassium hydroxide, 10 g.) for 2 hours, the solution poured into water, and the ketone extracted with ether. Removal of the ether left the tetralone as an oil, b. p. 165—173°/17 mm., from which were prepared the *semicarbazone*, which separated from aqueous alcohol in rhombic leaflets, decomp. 180—182° (Found : C, 69·7; H, 8·3. $C_{15}H_{21}ON_3$ requires C, 69·5; H, 8·1%), and the 2 : 4-*dinitrophenylhydrazone*, crystallising from butyl alcohol in orange-red needles, m. p. 235—236° (Found : C, 62·8; H, 5·9. $C_{20}H_{22}O_4N_4$ requires C, 62·8; H, 5·8%).

1 : 3-*Dimethyl*-7-iso*propylnaphthalene.*—The product (7·6 g.) obtained by treatment of 3-methyl-7-*iso*propyl-1 : 2 : 3 : 4-tetral-1-one with methylmagnesium iodide (from methyl iodide 16·3 g., magnesium 2·8 g.) in the usual manner, was heated with selenium (10 g.) at 300° for 24 hours. The oil was dissolved in ether, washed with sodium hydroxide solution, and dried. Removal of the ether left the naphthalene derivative (6·0 g.), b. p. 165—167°/19 mm. The *picrate* crystallised from alcohol in short orange needles, m. p. 102·5—104° (Found : C, 58·9; H, 5·0. $C_{15}H_{18},C_6H_3O_7N_3$ requires C, 59·0; H, 4·9%). The s-*trinitrobenzene* derivative crystallised from ethyl alcohol in yellow needles, m. p. 117—119°, completely molten at 121° (Found : C, 60·8; H, 5·3. $C_{15}H_{18},C_6H_3O_6N_3$ requires C, 61·3; H, 5·1%). The two derivatives were identical (m. p. and mixed m. p.) with the derivatives of the hydrocarbon obtained from hydroxymethylene-α-cyperone.

The description of a picrate, m. p. 113—114·5°, and a *s*-trinitrobenzene derivative, m. p. 141—142°, as derivatives of 1 : 3-dimethyl-7-*iso*propylnaphthalene, previously given (*loc. cit.*), is now withdrawn. In a subsequent communication it will be shown that these substances are derivatives of 1 : 5-dimethyl-7-*iso*propylnaphthalene.

We are indebted to the Government Grants Committee of the Royal Society and to the Chemical Society for grants.

UNIVERSITY COLLEGE OF N. WALES, BANGOR. [*Received, March 8th, 1937.*]

153. *The Oxidation of Some Polyhydroxylic and Polyethylenic Higher Fatty Acids by Aqueous Alkaline Permanganate Solutions.*

By T. G. Green and T. P. Hilditch.

Lapworth and Mottram (J., 1925, **127**, 1987) showed that when 9 : 10-dihydroxystearic acid (m. p. 131°) is oxidised by dilute aqueous alkaline permanganate under specified conditions, octoic, oxalic and suberic acids are produced by scission of the carbon chain between the 8 : 9 and the 10 : 11 carbon atoms :

$$CH_3\cdot[CH_2]_6\cdot CH_2 \vdots CH(OH)\cdot CH(OH) \vdots CH_2\cdot[CH_2]_6\cdot CO_2H$$
$$CH_3\cdot[CH_2]_6\cdot CO_2H \qquad CO_2H\cdot CO_2H \qquad HO_2C\cdot[CH_2]_6\cdot CO_2H$$

No scission of the carbon chain between the 9 : 10 carbon atoms, resulting in the formation of azelaic and nonoic acids, takes place. We have confirmed the observations of Lapworth and Mottram and have applied their procedure to other di-, tetra- and hexa-hydroxy-fatty acids and to α- and β-elæostearic acids. We find that the same type of oxidation occurs almost, if not wholly, exclusively in all the dihydroxy-acids which we have studied. These include the isomeric pairs of 9 : 10-dihydroxystearic acid (m. p.'s 131° and 95°), 9 : 10-dihydroxypalmitic acid (m. p.'s 123—124° and 83°), and 13 : 14-dihydroxybehenic acid (m. p.'s 128° and 100°) and also one of the 6 : 7-dihydroxystearic acids (m. p. 122°). *The course of the oxidation is thus independent of the stereoisomeric form of the dihydroxy-acid, of the length of the chain of carbon atoms present, or of the position of the hydroxyl groups in the carbon chain. Further, oxidation of the 13 : 14-dihydroxybehenic acids at different temperatures has established that the course of the oxidation is not affected by the temperature at which it is performed. In no case was any evidence observed of direct* scission between the two carbon atoms carrying the hydroxyl groups with formation of one monobasic and one dibasic acid.

In most cases attention was focused on the identity and yield of the dicarboxylic acid products of oxidation. Suberic (but no azelaic) acid was obtained from both 9 : 10-dihydroxystearic and 9 : 10-dihydroxypalmitic acids; decane-1 : 10-dicarboxylic acid (but no undecane-1 : 11-dicarboxylic acid) was obtained from both the 13 : 14-dihydroxybehenic acids at various temperatures; whilst glutaric and undecanoic acids were isolated from the oxidised 6 : 7-dihydroxystearic acid.

The stability of the dihydroxy-acids to oxidation in the cold by alkaline permanganate varied considerably. The 9 : 10-dihydroxystearic acids, the 9 : 10-dihydroxypalmitic acids and the 6 : 7-dihydroxystearic acid were all oxidised readily under the conditions employed. The 13 : 14-dihydroxybehenic acids, however, were very resistant and were only oxidised to a very small extent, even after 24 hours' treatment instead of the usual 2½ hours. It has previously been found (Green, Hilditch, and Stainsby, J., 1935, 1754) that 11 : 12-dihydroxyeicosanoic acid is much more resistant to oxidation than 9 : 10-dihydroxystearic acid, but it is attacked more readily than the 13 : 14-dihydroxybehenic acids. It would therefore seem that resistance of these acids to oxidation increases with increasing distance of the hydroxyl groups from the carboxyl group.

In the next place we examined the oxidation under similar conditions of the pairs of tetra- and hexa-hydroxystearic acids which are produced by mild oxidation with alkaline permanganate of the $\Delta^{9:12}$-octadecadienoic (linoleic) and the $\Delta^{9:12:15}$-octadecatrienoic (linolenic) acids of seed fats. In each of these we found that the dicarboxylic acids produced consisted largely of azelaic acid, accompanied, however, by about 20% of suberic acid; approximately the same proportion of suberic acid was present in the products from each of the hydroxy-acids.

We did not attempt to isolate hydroxy-acids from α- and β-elæostearic acids, but in these instances treated the unsaturated acids themselves with sufficient permanganate to decompose them. The dibasic acids produced consisted of a mixture of approximately 20% of suberic acid and 80% of azelaic acid in each case.

In all the Δ^9-polyethenoid C_{18} acids thus investigated, therefore, the carbon chain is split so that the dibasic (azelaic) acid with nine carbon atoms is the main product, but

that with one carbon atom less (suberic acid) nevertheless forms about 20% of the total dicarboxylic acids.

Farmer *et al.* have employed oxidation with alkaline permanganate in the identification of α-elæostearic acid in the seed fat of *Parinarium Macrophyllum* (J., 1935, 1760) and of β-elæostearic acid from an old specimen of oil from seeds of *Telfairia occidentalis* (*ibid.*, p. 1630) and in both these cases obtained azelaic and valeric acids as the oxidation products. Their conditions of oxidation were different from ours, the chief difference being in the amount of alkali present. Lapworth and Mottram (whose procedure we followed closely) recommended the use of a weight of caustic soda equal to twice the weight of hydroxy-acid being oxidised, *i.e.*, fourteen times the amount required to neutralise the acid. Farmer used a weight of sodium carbonate equal to approximately half the weight of unsaturated acid, *i.e.*, three times the amount required to neutralise the acid.

Whilst our present results show that alkaline permanganate oxidation of Δ^9-polyethenoid C_{18} acids leads to products in which azelaic acid is present in great excess over suberic acid, the amount of the latter is by no means insignificant and it would appear that alkaline permanganate oxidation as an aid in determining the position of ethylenic linkages in long-chain compounds might not, in certain cases, yield unequivocal information. In this respect it appears to compare unfavourably with oxidation by ozone or by anhydrous potassium permanganate in acetone solution.

Experimental.

Oxidation of the Dihydroxy-acids.

The conditions employed were very similar to those of Lapworth and Mottram (*loc. cit.*) except that the concentrations of the aqueous solutions were somewhat greater. This slight increase had no effect on the course of the oxidation, as is proved by the products obtained from 9 : 10-dihydroxystearic acid (m. p. 131°).

The dihydroxy-acid (5 g.) and caustic potash (14 g.) were dissolved in water (2000 c.c.), and the solution cooled to 0°. A solution of potassium permanganate (20 g.) in water (1500 c.c.) at 0° was added. After standing for 2½ hours at room temperature, the solution was decolorised by sulphur dioxide and concentrated hydrochloric acid (100 c.c.) was added. Any unchanged dihydroxy-acid was removed by filtration and washed with a little light petroleum to remove traces of liquid products of oxidation. The aqueous filtrate was neutralised with sodium carbonate and evaporated to about 500 c.c. It was then acidified with excess of hydrochloric acid and the oxidation products were extracted with ether. After recovery from the ether these products were distilled in steam to remove the monobasic acids. The dibasic acids crystallised from the aqueous residue on cooling, and in general were purified by recrystallisation from chloroform. Suberic acid is only very slightly soluble in chloroform, but that part of the crude acid which did not dissolve during treatment with this solvent was generally found to be fairly pure. If necessary, the suberic acid was submitted to further crystallisation from water.

The steam distillate was thoroughly extracted with ether and the light petroleum washings were added; the ethereal solution was then dried over anhydrous sodium sulphate for a week. When the monobasic acids were recovered the last traces of ether were removed under reduced pressure at 30—40°. It was, however, found to be practically impossible to remove the last traces of water from them. As the amount of these acids available was not sufficient for fractional distillation, the figures obtained for their equivalents cannot be regarded as trustworthy.

9 : 10-*Dihydroxystearic Acid* (*m. p.* 131°).—5 G. gave 2·20 g. of crude suberic acid, from which 1·87 g. (m. p. 135—139°) were obtained on recrystallisation (calc. for $C_8H_{14}O_4$, 2·75 g.). The monobasic acid weighed 2·0 g. (Found : equiv., 146·7. Calc. for $C_8H_{16}O_2$: 2·33 g.; equiv., 144).

9 : 10-*Dihydroxystearic Acid* (*m. p.* 95°).—5 G. gave 2·13 g. of crude suberic acid, from which 1·63 g. (m. p. 135—138°) were obtained by recrystallisation.

9 : 10-*Dihydroxypalmitic Acid* (*m. p.* 123—124°).—2·2 G. gave 0·94 g. of crude suberic acid (m. p. 131—137°), from which 0·75 g. (m. p. 138—140°) was obtained (Found : equiv., 87·4. Calc. for $C_8H_{14}O_4$: 1·33 g.; equiv., 87).

9 : 10-*Dihydroxypalmitic Acid* (*m. p.* 84°).—2·2 G. gave 0·97 g. of crude suberic acid (m. p. 130—137°), from which 0·72 g. (m. p. 138—140°) was obtained (Found : equiv., 88·0. Calc. for $C_8H_{14}O_4$: 1·33 g.; equiv., 87).

6 : 7-Dihydroxystearic Acid (*m. p.* 120—122°).—5 G. of the acid were oxidised. In this case the monobasic acid was a solid, insoluble in water, and after decolorisation and acidification was removed by filtration and separated from unchanged dihydroxy-acid (0·26 g.) by treatment with light petroleum. The recovered acid weighed 1·61 g. (Found: equiv., 187·1. Calc. for $C_{11}H_{22}O_2$: 2·8 g.; equiv., 186) and after recrystallisation from 70% alcohol melted at 28° [mixed with authentic undecanoic acid (m. p. 29°) at 28°].

The dibasic acid was very soluble in water and only about 1 g. was recovered (Found: equiv., 66·9. Calc. for $C_5H_8O_4$: 2·1 g.; equiv., 66). After two recrystallisations from benzene it melted at 91—94° (Found: C, 46·5; H, 6·2. Calc. for $C_5H_8O_4$: C, 45·5; H, 6·1%).

13 : 14-Dihydroxybehenic Acid (*m. p.* 127—129°).—The dibasic acid obtained in this case was only very slightly soluble in cold water. Consequently, when the oxidations had been carried out, the acids which were filtered off contained some dibasic acid. This was separated from the unchanged dihydroxy-acid by boiling with water.

2·2 G. were oxidised at room temperature for 24 hours. 1·81 G. were recovered unchanged, together with 0·07 g. of dibasic acid which melted at 127° after recrystallisation from chloroform [mixed with decane-1 : 10-dicarboxylic acid (m. p. 127°) at 127°; mixed with dihydroxybehenic acid (m. p. 127—129°) at 114—116°] (Found: C, 62·8; H, 9·0. Calc. for $C_{12}H_{22}O_4$: C, 62·6; H, 9·6%).

1·4 G. were oxidised at 60° for 2 hours, then overnight at room temperature. 0·90 G. was recovered unchanged, together with 0·07 g. of dibasic acid melting at 125—126° [mixed with decane-1 : 10-dicarboxylic acid (m. p. 127°) at 126°].

13 : 14-Dihydroxybehenic Acid (*m. p.* 100°).—2·2 G. were oxidised for 24 hours at room temperature. 1·55 G. were recovered unchanged, together with 0·05 g. melting at 123° [mixed with decane-1 : 10-dicarboxylic acid (m. p. 127°) at 124—126°].

When 2·2 g. were oxidised at 100° for 4 hours, 0·63 g. of crude decane-1 : 10-dicarboxylic acid was obtained. By recrystallisation from chloroform, 0·37 g. melting at 124—126° was separated [mixed with decane-1 : 10-dicarboxylic acid (m. p. 127°) at 125—126°] (Found: equiv., 115·1. Calc. for $C_{12}H_{22}O_4$: equiv., 115).

Oxidation of the Tetrahydroxystearic Acids.

The tetrahydroxystearic acids were oxidised under the same conditions as the dihydroxy-acids except that the amounts of permanganate and alkali were doubled. The same procedure was adopted to recover the products, and, since azelaic acid is very much more soluble in chloroform than suberic acid, the two acids were readily separated by using this solvent.

Tetrahydroxystearic Acid (*m. p.* 155°).—5 G. gave three crops of crude dibasic acids: 0·78 g. (m. p. 94—95°), 1·00 g. (m. p. 103—115°), 0·21 g. (m. p. 100—120°). These were separated into 0·37 g. melting at 136—138° [mixed with suberic acid (m. p. 139°) at 136—138°], and 1·27 g. melting at 97—98° [mixed with azelaic acid (m. p. 105°) at 97—102°] (Found: equiv., 94·7. Calc. for $C_9H_{16}O_4$: equiv., 94).

Yield of suberic acid compared with the total yield of dibasic acids *: 18·5%.

The monobasic acids weighed 1·34 g. (Found: equiv., 117·7. Calc. for $C_6H_{12}O_2$: equiv., 116. Calc. for $C_5H_{10}O_2$: equiv., 102).

Tetrahydroxystearic Acid (*m. p.* 173°).—5 G. gave two crops of crude dibasic acids: 0·93 g. (m. p. 94—105°), 0·90 g. (m. p. 104—115°). These were separated into 0·44 g. melting at 136—138° (Found: equiv., 86·2. Calc. for $C_8H_{14}O_4$: equiv., 87) and 0·90 g. melting at 97—98° (Found: equiv., 93·8. Calc. for $C_9H_{16}O_4$: equiv., 94).

Yield of suberic acid compared with total yield of dibasic acids: 24%.

The monobasic acids weighed 1·60 g. (Found: equiv., 115·5).

Oxidation of the Hexahydroxystearic Acids.

When the hexahydroxystearic acids were oxidised with the same proportion of permanganate as the tetrahydroxystearic acids, no appreciable amount of acid remained unattacked; accordingly, in these cases the amount of permanganate was not further increased.

Hexahydroxystearic Acid (*m. p.* 204°).—3 G. gave two crops of dibasic acids: 0·83 g. (m. p. 85—95°) and 0·24 g. (m. p. 108—123°). These were separated into 0·17 g. melting at 137—139° (Found: equiv., 87·0), 0·37 g. melting at 98—102° (Found: equiv., 94·8) and 0·15 g. melting at 102—103°.

Yield of suberic acid compared with the total yield of dibasic acids: 16%.

* This method of stating the proportion of suberic acid is employed because, owing to the appreciable solubility of azelaic acid in chloroform, the recovery of the latter acid was not quantitative.

Hexahydroxystearic Acid (*m. p.* 169°).—4·3 G. of the acid gave two crops of dibasic acids: 1·05 g. (m. p. 105—120°) and 0·47 g. (m. p. 95—120°). These were separated into 0·37 g. melting at 136—138° (Found: equiv., 86·1) and 0·52 g. melting at 95—102° (Found: equiv., 93·2).

Yield of suberic acid compared with the total yield of dibasic acids: 24%.

Oxidation of α- and β-Elæostearic Acids.

These acids were oxidised in the same way as the dihydroxy-acids except that three times as much permanganate and alkali were used. Under these conditions no difficulty in obtaining complete oxidation was encountered.

α-Elæostearic Acid (*m. p.* 45—46°).—5 G. gave two crops of dibasic acids: 1·71 g. (m. p. 93—108°) and 0·65 g. (m. p. 105—115°). These were separated into 0·57 g. melting at 135—138° (Found: equiv., 86·1) and 1·29 g. melting at 95—102° (Found: equiv., 95·1).

Yield of suberic acid compared with the total yield of dibasic acids: 24%.

The monobasic acids weighed 0·96 g. (Found: equiv., 101·4. Calc. for $C_5H_{10}O_2$: equiv., 102. Calc. for $C_4H_8O_2$: equiv., 88).

β-Elæostearic Acid (*m. p.* 70°).—5 G. gave two crops of crude dibasic acids: 1·85 g. (m. p. 93—111°) and 0·60 g. (m. p. 103—115°). These were separated into 0·42 g. melting at 135—138° and 0·72 g. melting at 98—102°.

Yield of suberic acid compared with the total yield of dibasic acids: 17%.

The monobasic acids weighed 1·53 g. (Found: equiv., 102·9).

SUMMARY.

(1) 9 : 10-Dihydroxystearic acid (m. p. 131°), as previously observed by Lapworth and Mottram (*loc. cit.*), gives suberic, octoic and oxalic acids when oxidised with aqueous alkaline permanganate under specified conditions. This type of oxidation has now been found to occur under similar conditions with 9 : 10-dihydroxystearic acid (m. p. 95°), 9 : 10-dihydroxypalmitic acids (m. p.'s 123—124° and 83°), 13 : 14-dihydroxybehenic acids (m. p.'s 128° and 100°) and 6 : 7-dihydroxystearic acid (m. p. 122°). The course of the oxidation is thus independent of the stereoisomeric form of the acid, the length of the carbon chain or the position of the adjacent hydroxyl groups in the chain. Temperature exerts no influence on the course of the oxidation. The resistance of the dihydroxy-acids to oxidation increases with increasing distance between the carboxyl and the hydroxyl groups.

(2) When the tetrahydroxystearic acids (m. p.'s 155° and 173°) and the hexahydroxystearic acids (m. p.'s 169° and 203°) were oxidised under similar conditions, the dicarboxylic acids produced consisted mainly of azelaic acid accompanied, however, by about 20% of suberic acid.

(3) The dibasic acids resulting from the degradation of α- and β-elæostearic acids by aqueous alkaline permanganate consisted of approximately 80% of azelaic acid and 20% of suberic acid.

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154. *Some Unsaturated Sulphides derived from the Chloroethylenes.*

By N. W. CUSA and H. MCCOMBIE.

THE reactivity of a halogen atom attached to a carbon atom adjacent to a double bond is very limited. Displacement has been brought about only by means of vigorous treatment with alkali hydroxide or alkoxide, by alcoholic alkali-metal mercaptides, and by aromatic bases in the presence of alkali.

Thus dichloroethylene, when heated with alcoholic potash, affords chloroacetylene (Hofmann and Kirmreuther, *Ber.*, 1909, **42**, 4233), and when heated with alkali mercaptides in alcoholic solution it readily gives rise to dialkyl- or diaryl-substituted dithioethylenes

(Fromm and others, *Annalen*, 1912, **394**, 325; *Ber.*, 1922, **55**, 1014). Di-(*o*-carboxyphenylthio)ethylene has been obtained by the action of dichloroethylene on sodium thiosalicylate (Münsch, *Z. angew. Chem.*, 1908, **21**, 2059; Bohn, *Ber.*, 1910, **43**, 994).

Trichloroethylene, when heated with alcoholic potash, affords αβ-dichlorovinyl ethyl ether (Paternò and Oglialoro, *Ber.*, 1874, **7**, 81; D.R.-P. 216,940) and it is readily converted by mineral acids into chloroacetic acid (Simon and Chavanne, *Compt. rend.*, 1923, **176**, 309; D.R.-PP. 359,910, 377,524, 383,029, etc.). It reacts with aniline in the presence of alkali to give phenylglycinediphenylamidine (Ruggli and Marszak, *Helv. Chim. Acta*, 1928, **11**, 180). Tribromoethylene, when treated with alcoholic potassium phenoxide (Ssabanejew and Dworkowitsch, *Annalen*, 1883, **216**, 280), gives first phenyl ββ-dibromovinyl ether and finally phenoxyacetic acid. D.R.-P. 210,644 reports a product obtained by the interaction of trichloroethylene and thiosalicylic acid, and ascribes to it the constitution $CCl_2{:}CH{\cdot}S{\cdot}C_6H_4{\cdot}CO_2H$.

Tetrachloroethylene, heated with sodium ethoxide at 100—120°, yields, together with other products, ethyl dichloroacetate (Geuther and others, J., 1864, **17**, 316; 1873, **26**, 314). When treated with *o*-dithiolbenzene in a sealed tube at 110—120° for 7 hours, it gives rise to the indigoid compound $C_6H_4{<}^{S}_{S}{>}C{:}C{<}^{S}_{S}{>}C_6H_4$ (Hartley and Smiles, J., 1926, 2263).

Experiments have now been carried out on the reaction of ethyl mercaptan, monothioethylene glycol, and of thiophenol with these substances under various conditions. It has been found that dichloroethylene very readily gives rise to a disubstituted compound with thiophenol and with ethyl mercaptan, but does not react readily with monothioethylene glycol. Even in the presence of a large excess of dichloroethylene no chlorovinylthio-compound could be isolated.

Dichloroethylene reacts with an alcoholic solution of sodium sulphide, but the product is not ββ′-dichlorodivinyl sulphide, but a resinous polymer.

Attempts have been made to bring about the interaction of acetylene and sulphur monochloride and dichloride without success. A mixture of αα′- and ββ′-dichlorodivinyl sulphides has been obtained by thermal decomposition of αβα′β′-tetrachlorodiethyl sulphide. This decomposition was reported by Kliger (*J. Gen. Chem.*, Vol. III, LXV, No. 8), but we find that, contrary to Kliger's statements, the tetrachloro-compound is sufficiently stable to distil at 15 mm. (cf. Alexander and McCombie, J., 1931, 1913), although when heated at ordinary pressures it loses hydrogen chloride and gives rise to a liquid, b. p. 75—80°/15 mm., which appears to be a mixture of dichlorodivinyl sulphides. This product does not give a crystalline sulphilimine when treated with chloramine-T, but it reacts readily with alcoholic solutions of sodium thiophenoxide and sodium β-naphthoxide, giving oily products from which crystalline fractions were obtained. Attempts have been made to determine the constitution of the thiophenol derivative by reduction to known compounds, but this was not achieved. Catalytic reduction in neutral solution could not be effected, and acid or alkaline reagents either had no effect or brought about a fission of the molecule with formation of thiophenol. The action of sodium in alcohol brought about its conversion into what seemed to be a geometrical isomeride.

Di-iodoethylene reacts with alcoholic solutions of alkali-metal mercaptides, giving rise to acetylene and the disulphide.

Trichloroethylene reacts smoothly in alcoholic solution with one molecule of sodium thiophenoxide, giving rise to a dichloro-compound, C_2HCl_2SPh, in good yield. The constitution of this compound is of interest in view of the conflicting constitutions assigned to the ethyl derivative (Paternò and Oglialoro, *loc. cit.*), the phenoxy-derivative of tribromoethylene (Ssabanejew and Dworkowitsch, *loc. cit.*), and the carboxyphenylthio-derivative (D.R.-P. 210,644). Evidence has been obtained which will admit only of the *phenyl αβ-dichlorovinyl sulphide* structure. Thus, although no further chlorine atom can be displaced by further treatment with thiophenol, one, and one only, can be brought into reaction with sodium methoxide, suggesting their unsymmetrical disposition. A *tetrachloro*-derivative is formed smoothly when the substance is treated with chlorine in carbon tetrachloride; there is no evidence that this contains the CCl_3 group. Finally, it is slowly decomposed by boiling aqueous caustic alkali, giving thiophenol and glycollic acid.

In contrast to these results, evidence has been obtained that all three chlorine atoms of trichloroethylene can be displaced by the ethylthio-group by means of ethyl mercaptan.

Tetrachloroethylene reacts with two molecular proportions of sodium thiophenoxide in alcoholic solution to give what is, in all probability, the symmetrical *compound*, SPh·CCl:CCl·SPh, which should be capable of existing in *cis*- and *trans*-isomeric forms. No evidence of isomerism was observed in this case, but, by the interaction of tetrachloroethylene and monothioethylene glycol and treatment of the hydroxy-compounds so formed with thionyl chloride, two compounds were obtained, each a tetrachloro-compound, which may have been geometrically isomeric substances of the symmetrical structure CH_2Cl·CH_2·S·CCl:CCl·S·CH_2·CH_2Cl.

EXPERIMENTAL.

Diphenylthioethylene.—Sodium (1 atom) was dissolved in absolute alcohol and thiophenol (1 mol.) was added immediately, followed by dichloroethylene (0·5 mol.). The mixture was heated under reflux during 24 hours and sodium chloride, which separated slowly, was removed. The filtrate was evaporated, and the residue poured into water. The oily layer was dried and distilled, b. p. 235—242°/760 mm.; it solidified when cold and on crystallisation from light petroleum afforded colourless plates, m. p. 62° (Found: C, 68·5; H, 5·05. $C_{14}H_{12}S_2$ requires C, 68·8; H, 4·92%). There was a little oily by-product.

Dichlorodivinyl Sulphide.—αβα′β′-Tetrachlorodiethyl sulphide (Alexander and McCombie, *loc. cit.*), when distilled at atmospheric pressure, decomposed with evolution of hydrogen chloride. The distillate, b. p. 75—80°/15 mm. after redistillation, was a colourless, unpleasantly smelling liquid which darkened when kept (Found: Cl, 46·6. $C_4H_4Cl_2S$ requires Cl, 45·8%). The chlorine could not be completely replaced by iodine by means of methyl-alcoholic sodium iodide.

Di(phenylthio)divinyl Sulphide.—Sodium (1 atom) was dissolved in absolute alcohol, thiophenol (1 mol.) added, and the solution warmed under reflux with dichlorodivinyl sulphide (0·5 mol.). After 1 hour sodium chloride and an oil had separated. The oil solidified to a crystalline solid on cooling and shaking. This was separated by filtration and freed from sodium chloride by extraction with cold water. Recrystallised from hot alcohol, it formed colourless plates, m. p. 78°. This substance was halogen-free and unsaturated towards bromine (Found: C, 63·3; H, 4·9. $C_{16}H_{14}S_3$ requires C, 63·6; H, 4·6%).

Addition of water to the alcoholic filtrate precipitated quantities of halogen-free oil, from which no further crystalline substance could be isolated.

Isomeric Di(phenylthio)divinyl Sulphide.—In the course of experiments designed to convert the di(phenylthio)divinyl sulphide into known derivatives of diethyl sulphide, the substance (1 g.) was dissolved in absolute alcohol (50 c.c.), and an excess (1 g.) of sodium added. The solution, which became turbid, was filtered; the filtrate, on standing, deposited small shining plates, m. p. 128—140°, which, when recrystallised from aqueous acetone, had m. p. 138°. Analysis, together with the fact that the substance was still unsaturated towards bromine, showed that reduction had not taken place. It is suggested that the product was a geometrical isomeride of the original sulphide (Found: C, 63·1; H, 4·75. $C_{16}H_{14}S_3$ requires C, 63·6; H, 4·6%. $C_{16}H_{18}S_3$ requires C, 62·7; H, 5·6%).

Di-(β-naphthyloxy)divinyl Sulphide.—This substance was prepared in poor yield by adding β-naphthol (2 mols.) to sodium (2 atoms), dissolved in absolute alcohol, and heating the mixture with dichlorodivinyl sulphide (1 mol.) during 3 hours. Sodium chloride separated. The alcoholic filtrate, on standing overnight, gave a further small deposit, which, recrystallised from hot acetone, afforded colourless plates, m. p. 151—152° (Found: C, 77·1; H, 4·7. $C_{24}H_{18}O_2S$ requires C, 77·8; H, 4·75%).

Phenyl αβ-Dichlorovinyl Sulphide.—Trichloroethylene (1 mol.) was added to a solution of sodium (1·2 atoms) and thiophenol (1·2 mols.) in absolute alcohol. The mixture was heated under reflux during 24 hours; sodium chloride (1 mol.) had then separated. The *product*, isolated and distilled, was a colourless liquid, b. p. 145—150°/22 mm. (Found: Cl, 34·7. $C_8H_6Cl_2S$ requires Cl, 34·6%). The use of an excess of thiophenoxide afforded the same product.

Phenyl α-Chloro-β(?)-methoxyvinyl Sulphide.—The preceding sulphide was heated at 100° during 6 hours with solid sodium methoxide in excess (3 mols.). The *product* was filtered, poured into water, separated, dried, and distilled. It was a pale yellow oil, b. p. 160—165°/20 mm. (Found: Cl, 14·8. C_9H_9OClS requires Cl, 15·4%).

Phenyl ααββ-Tetrachloroethyl Sulphide.—Phenyl αβ-dichlorovinyl sulphide was dissolved in

carbon tetrachloride, and a trace of iodine added. Chlorine was passed through the solution, kept at 0°, until absorption ceased. The *product*, when distilled, afforded a pale yellow oil, b. p. 175—182°/20 mm. (Found: Cl, 46·8. $C_8H_6Cl_4S$ requires Cl, 44·3%). The high chlorine figure, together with the evolution of a little hydrogen chloride during chlorination, points to the occurrence of some substitution. When the substance was boiled with acid or alkali, no trace of chloroform could be detected among the products: it therefore probably does not contain the trichloromethyl group. On standing, it rapidly loses hydrogen chloride, giving, possibly, phenyl αββ-trichlorovinyl sulphide.

Action of Alkali on Phenyl αβ-Dichlorovinyl Sulphide.—The substance (5 g.) was treated with 10% aqueous caustic soda (100 c.c.) and sufficient ethyl alcohol to produce a homogeneous solution. The mixture was heated under reflux during 3 hours, the alcohol distilled, and the residue acidified, distilled in steam to remove thiophenol, and evaporated to dryness. The product, containing sodium chloride, was completely soluble in water, reduced alkaline potassium permanganate only slowly, when warmed, and gave no precipitate with ammonium oxalate. It was therefore free from oxalic acid and from glyoxal. The presence of glycollic acid was shown by preparation of the phenylurethane. The mixture (2·3 g.) was heated with an excess (4 g.) of phenyl *iso*cyanate at 130° for 3 hours. Water was then added and the insoluble portion was fractionally crystallised from alcohol, giving carbanilide (m. p. 236°) and a substance, sparingly soluble in water, soluble in aqueous alkali, m. p. (after three crystallisations) 143° (cf. Lambling, *Compt. rend.*, 1868, **66**, 1276; Fischer, *Ber.*, 1914, **47**, 775).

Trichloroethylene and Ethyl Mercaptan.—Sodium (1 atom) was dissolved in absolute alcohol and ethyl mercaptan (1 mol.) was added, followed by trichloroethylene (1 mol.). The mixture was heated under reflux for 2 hours; sodium chloride (1 mol.) had then separated. The filtrate was poured into an excess of water and the oil which separated was dried and distilled. It boiled over a very wide range (70—150°/20 mm.) and was further fractionated through a column: Fraction (1), b. p. 77—80°/30 mm. (Found: Cl, 42·7%); fraction (2), b. p. 135—140°/20 mm. [Found: Cl, 12·8. C_2HCl_2·SEt requires Cl, 45·2%. $C_2HCl(SEt)_2$ requires Cl, 19·5%]. It is evident, therefore, that whilst fraction (1) is a fairly pure monosubstituted derivative, fraction (2) contains a considerable proportion of the trisubstituted product $C_2H(SEt)_3$. This affords an interesting contrast to the action of thiophenol.

s-*Dichlorodiphenylthioethylene.*—Sodium thiophenoxide (2 mols.) in alcohol was treated with tetrachloroethylene (1 mol.). Sodium chloride (2 mols.) separated after 48 hours' heating under reflux. This was removed; the alcoholic filtrate, on standing, deposited colourless needles, which, recrystallised twice from alcohol, had m. p. 71—72° (Found: C, 53·7; H, 3·4. $C_{14}H_{10}Cl_2S_2$ requires C, 53·6; H, 3·2%).

No other product was isolated. This *compound* was recovered unchanged after heating during 5 hours under reflux in alcohol in presence of an excess of sodium thiophenoxide.

Tetrachloroethylene and Monothioethylene Glycol.—Sodium (1 atom) was dissolved in absolute alcohol and monothioethylene glycol (1 mol.) was added, followed by tetrachloroethylene (0·5 mol.). Reaction was complete and sodium chloride (1 mol.) was filtered off after 2 hours' boiling. The alcohol was distilled from the filtrate and the semi-solid residue was dried and boiled with thionyl chloride (2 mols.) during 30 minutes. The product was distilled, a colourless oil being collected at 150—160°/35 mm. (a) and a dark brown liquid passing over between 160° and 230° which solidified when cooled in ice (b). Product (a) was redistilled and collected at 145—147°/30 mm. (Found: Cl, 48·7. $C_6H_8Cl_4S_2$ requires Cl, 48·5%). Product (b), pressed on porous earthenware and crystallised from light petroleum, afforded colourless prisms, m. p. 72—73°, containing sulphur and chlorine (Found: C, 25·7; H, 3·0. $C_6H_8Cl_4S_2$ requires C, 25·2; H, 2·8%). Neither of these compounds absorbed bromine readily.

THE UNIVERSITY CHEMICAL LABORATORY, CAMBRIDGE. [*Received, March 9th*, 1937.]

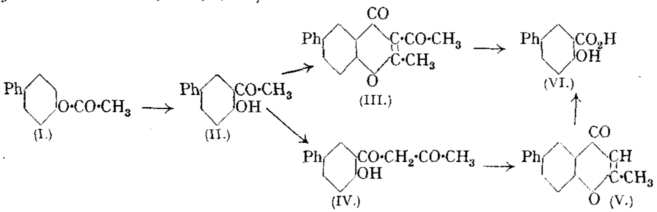
155. *Migration Reactions in Polycyclic Systems. Part II. The Fries Rearrangement of 4-Acetoxydiphenyl.*

By KENNETH H. CHEETHAM and DONALD H. HEY.

FIESER and BRADSHER (*J. Amer. Chem. Soc.*, 1936, **58**, 1738) have shown that the action of succinic anhydride on 4-methoxydiphenyl in the presence of aluminium chloride gives rise to substitution at both the 4'- and the 3-position, since the two products yield 4-hydroxydi-

phenyl-4′-carboxylic acid and 4-hydroxydiphenyl-3-carboxylic acid respectively on oxidation and demethylation. They also stated that the action of acetyl chloride on 4-methoxydiphenyl in the presence of aluminium chloride, under a variety of conditions, yields two products, namely, 4-methoxy-4′-acetyldiphenyl and 4-methoxy-3-acetyldiphenyl. The constitution of the former was proved by oxidation, but that of the latter was inferred by analogy to the corresponding reaction using succinic anhydride. Further, the action of aluminium chloride on 4-acetoxydiphenyl was stated to yield two isomeric hydroxyacetyldiphenyls, which gave on methylation the same two products which resulted from the Friedel–Crafts reaction on 4-methoxydiphenyl.

In Part I (Hey and Jackson, J., 1936, 802) it was shown that, contrary to the statement of Blicke and Weinkauff (*J. Amer. Chem. Soc.*, 1932, **54**, 330), the action of aluminium chloride on 4-benzoyloxydiphenyl gave rise to 4-hydroxy-3-benzoyldiphenyl, the constitution of which was proved by an unambiguous synthesis. A parallel investigation into the course followed by the corresponding reaction with 4-acetoxydiphenyl was in hand at the time of the publication of Fieser and Bradsher's communication. Under our experimental conditions the action of aluminium chloride on 4-acetoxydiphenyl (I) yields only 4-hydroxy-3-acetyldiphenyl (II), which appears to have been the main product of the reaction as carried out by Fieser and Bradsher. Moreover, the constitution of this compound is proved conclusively without recourse to the method of independent synthesis necessitated in Part I (*loc. cit.*), (a) by conversion into 3-*acetyl*-6-*phenyl*-2-*methylchromone* (III) by heating with a mixture of acetic anhydride and fused sodium acetate (cf. Baker, J., 1933, 1383; Chadha, Mahal, and Venkataraman, *ibid.*, p. 1459), and (b) by condensation with ethyl acetate in presence of sodium to yield a diketone (IV), which on ring closure gives 6-*phenyl*-2-*methylchromone* (V) (cf. Heilbron, Hey, and Lowe, J., 1934, 1311). Both the chromone (V) and the acetylchromone (III) yield 4-hydroxydiphenyl-3-carboxylic acid (VI) on treatment with hot aqueous alkali. The analogy drawn by Fieser and Bradsher is thus fully justified. The chromone (V) yields with benzaldehyde a *styryl* derivative in the normal manner (cf. Heilbron, Barnes, and Morton, J., 1923, **123**, 2559; Chakravarti, *J. Indian Chem. Soc.*, 1931, **8**, 129).



In a second communication, Fieser and Bradsher (*J. Amer. Chem. Soc.*, 1936, **58**, 2337) have turned their attention to the action of aluminium chloride on 4-benzoyloxydiphenyl in view of the fact that, as described in Part I (*loc. cit.*), this reaction was stated to yield only 4-hydroxy-3-benzoyldiphenyl. Under the experimental conditions used by these authors 4-hydroxy-4′-benzoyldiphenyl was obtained in 22% yield, a result similar to that described by Blicke and Weinkauff (*loc. cit.*), although it is stated that this compound could not be obtained under Blicke and Weinkauff's conditions (cf. Part I). These discrepancies are probably accounted for by variations in experimental conditions and in the methods of separating the products (cf. Short, Stromberg, and Wiles, J., 1936, 319).

Experimental.

4-Acetoxydiphenyl (I) was prepared in quantitative yield by boiling under reflux 4-hydroxydiphenyl (cf. Part I) with acetic anhydride and one drop of concentrated sulphuric acid and pouring the mixture into water; after crystallisation from 95% alcohol, it melted at 87—88° (cf. Kaiser, *Annalen*, 1890, **257**, 102).

Action of Aluminium Chloride on 4-Acetoxydiphenyl.—A solution of 4-acetoxydiphenyl (10·5 g.) in dry tetrachloroethane (75 c.c.) was heated with finely powdered aluminium chloride (7·5 g.) at 140° in an oil-bath for 2 hours. The cold product was treated with ice and hydrochloric acid and the tetrachloroethane was removed with steam. The non-volatile residue was extracted several times with hot aqueous sodium hydroxide and the solid, which was precipitated on acidification of the filtered extract, was dried and extracted with hot benzene. Evaporation of the benzene left a viscous residue, which was subjected to fractional crystallisation from light petroleum (b. p. 40—60°). Some 4-hydroxydiphenyl (m. p. and mixed m. p. 165° after crystallisation from aqueous alcohol) separated first, but on further concentration 4-hydroxy-3-acetyldiphenyl (II) was deposited in transparent, pale yellow prisms, m. p. 59—61°. Further crystallisation from the same solvent raised the m. p. to 61·5—62° (Found: C, 79·4; H, 6·0. Calc. for $C_{14}H_{12}O_2$: C, 79·2; H, 5·7%). On methylation with methyl iodide in acetone solution in the presence of potassium carbonate 4-methoxy-3-acetyldiphenyl, m. p. 62°, was obtained (cf. Fieser and Bradsher, *loc. cit.*, p. 1741).

Action of Sodium Acetate and Acetic Anhydride on 4-Hydroxy-3-acetyldiphenyl.—The hydroxyketone (1·5 g.) was heated in an oil-bath with a mixture of anhydrous sodium acetate (4 g.) and acetic anhydride (6 g.) at 120° for 2 hours and finally at 180° for 5 hours. Water was added to the cold product and, after standing overnight, the aqueous layer was decanted from a thick brown oil. The latter was boiled under reflux in alcoholic solution with the addition of a little charcoal and filtered. The clear solution deposited clusters of feathery needles and after further crystallisation from dilute alcohol *3-acetyl-6-phenyl-2-methylchromone* (III) was obtained in small white needles, m. p. 143·5° (Found: C, 77·9; H, 4·8. $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·0%).

6-Phenyl-2-methylchromone (V).—A solution of 4-hydroxy-3-acetyldiphenyl (1·25 g.) in dry ethyl acetate (10 c.c.) was added to powdered sodium (0·4 g.). After the addition of more ethyl acetate (10 c.c.) the mixture was warmed on the water-bath and finally boiled under reflux for ½ hour. The solution became yellow and a bright orange precipitate separated. The cold mixture was poured on ice (15 g.) and the precipitated sodium salt of the diketone (IV) was filtered off and washed with ice-water. When dry, it was dissolved in glacial acetic acid and, after the addition of three drops of concentrated hydrochloric acid, the solution was boiled for ½ hour to effect ring closure (cf. Baker, *loc. cit.*, p. 1382). The *chromone* (V), which was precipitated on the addition of water, was crystallised twice from ethyl alcohol, from which it separated in transparent flakes, m. p. 163·5° (Found: C, 81·7; H, 5·3. $C_{16}H_{12}O_2$ requires C, 81·4; H, 5·1%).

6-Phenyl-2-styrylchromone.—To a solution of 6-phenyl-2-methylchromone (0·1 g.) in absolute alcohol (15 c.c.) were added a solution of sodium (0·05 g.) in alcohol (10 c.c.), and benzaldehyde (0·1 g.). On standing at room temperature for 2 hours, a pale yellow precipitate separated from the red-yellow solution. Two crystallisations from absolute alcohol, to which a few drops of benzene had been added, yielded the *styryl* derivative in dull white flakes, m. p. 202·5° (Found: C, 84·7; H, 5·0. $C_{23}H_{16}O_2$ requires C, 85·2; H, 4·9%), soluble in hot benzene but sparingly soluble in alcohol.

Hydrolyses.—Both 3-acetyl-6-phenyl-2-methylchromone (III) and 6-phenyl-2-methylchromone (V) were boiled with aqueous sodium hydroxide. In both cases the solid gradually dissolved and subsequent acidification of the solution deposited a white precipitate of 4-hydroxydiphenyl-3-carboxylic acid (VI), which, after crystallisation from *cyclo*hexane–ether, was obtained in white needles, m. p. 210—211° (cf. U.S.P. 1,839,526 and 1,941,207; Fieser and Bradsher, *loc. cit.*, p. 1740). In very dilute alcohol it gave an intense blue-violet coloration with ferric chloride.

The University, Manchester. [*Received, March 13th*, 1937.]

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156. *Catalysed Polymerisation in Monolayers of Drying Oils.*

By G. Gee and Eric K. Rideal.

It has been shown (*Proc. Roy. Soc.*, 1935, *A*, 153, 116, 129) that monolayers of maleic anhydride β-elæostearin (X) when spread on acid substrates undergo a series of reactions in the process of "drying," comprising essentially an autoxidation involving an intermediary active form (XO_2') followed by the polymerisation of the products of oxidation (XO_2' and XO_2). Since the chains of the polymeric molecules are formed in the monolayer, we

might conclude that, if chain-stopping molecules were incorporated in the original ester as a mixed film, the polymerisation process would be retarded but the autoxidation reaction would remain unaffected. Further, if these chain-stopping molecules consisted of the esters of the unsaturated acids they would not be equally effective as chain stoppers since they would possess the possibility of being incorporated in the growing chain to form mixed polymers; various unsaturated esters should show different efficiencies as chain inhibitors, dependent on the ease with which they can be incorporated in the chain.

The acceleration or retardation of an autoxidation by addition of a catalyst may be considered from several points of view. Moureu and Dufraisse (*Chem. Rev.*, 1926, **3**, **113**; *Chem. and Ind.*, 1928, **47**, 819, 848) showed that the catalyst must be a substance which is itself capable of autoxidation. They postulated the existence of a transitory peroxide as the first oxidation product, and formulated the catalytic mechanism as the interaction of the peroxides of the two autoxidants with one another and with unoxidised material. In recent years their views have been overshadowed by the chain reaction theory elaborated by Christiansen, Bäckström, and others (cf. *e.g.*, Christiansen, *J. Physical Chem.*, 1924, **28**, 145; Bäckström, *J. Amer. Chem. Soc.*, 1927, **49**, 1460; *Medd. K. Vetenskapsakad. Nobel-Inst.*, 1927, **6**, Nos. 15, 16; Semenoff, "Chemical Kinetics and Chain Reactions"), but it must be noted that there is a very close relationship between the two points of view (Semenoff, *op. cit.*, p. 361). If the chain is considered to involve a free-radical mechanism, the analogy with classical ideas is less apparent, but we may say in general that all these formulations involve one essential idea. If we denote the two autoxidants by A, B, and their oxidation products by AO, BO, the autoxidation must be written

$$A \longrightarrow X \longrightarrow AO \qquad B \longrightarrow Y \longrightarrow BO$$

where X, Y represent one or more unstable intermediate substances. If B is regarded as the catalyst, its function is to change the concentration of X by reacting with it either in the form of unoxidised B or as Y. Quantitative differences between the classical and the chain formulation arise from the fact that removal of one molecule of X can, according to the former, prevent the formation of only one or two molecules of AO, whereas in the latter case, the number of molecules formed from a single X is equal to the chain length of the reaction.

We thus conclude that the effects of catalysts and inhibitors injected into the substrate in the oxidation and polymerisation stages should show important differences of mechanism. Oxidation catalysts, whether they function as suggested by Moureu or Duffaisse or through the formation of the HO_2 radical, *e.g.*

$$Co^{++} + O_2 \rightleftarrows Co^{+++} + O_2'$$
$$O_2' + H^+ \rightleftarrows HO_2$$

should form no complexes with the original material, whilst anti-oxidants reduce the primary oxidation product to its original state. It has been suggested elsewhere (*Trans. Faraday Soc.*, 1936, **32**, 666) that polymerisation catalysts should, on the other hand, form a complex with the polymerisable material (the peroxide), and polymerisation inhibitors should reduce the active monomer possibly to a lower stage of oxidation.

It has been shown (*ibid.*, p. 187) that the cobalt ion is a catalyst and quinol an inhibitor both for the oxidation and for the polymerisation process, but, that the two processes can be independently affected is shown by the fact that *p*-nitroaniline (0·01%) retards the oxidation without affecting the rate of polymerisation of XO_2, whilst a mixture of *p*-nitroaniline (0·01%) and iodoacetic acid (0·03%) retards the oxidation but accelerates the process of polymerisation when carried out on 0·01*N*-sulphuric acid as substrate.

The above conclusions as to the mechanism of catalysis are capable of being tested in a simple and direct manner by surface-potential measurements by observing the effect —if any—of injecting a catalyst into the substrate, whereupon complex formation would be indicated by a potential change.

The results of experiments with films of maleic anhydride β-elæostearin were as follows, blank experiments having shown that dilute solutions of cobalt sulphate and quinol were without effect on the potential difference.

(i) *Effect on unoxidised film.* Films were spread on 0·01*N*-sulphuric acid (*a*) alone; (*b*) with addition of 0·1% of quinol; (*c*) with addition of 0·005% of cobaltous ion (as sulphate), and the potentials measured (see *Proc. Roy. Soc.*, 1935, **153**, **116**, **129**) at a fixed surface pressure ($F = 9$ dynes/cm.). On substrate (*b*), the film was stable and its potential was readily measured; on the other substrates, reaction commenced at once and the potential was measured at intervals while the pressure was kept constant, the initial potential being subsequently determined by extrapolation to zero time. The results obtained in this way were subject to some error, but after a number of experiments it was concluded that the potential of the unoxidised film is not altered significantly by the presence in the substrate of either cobaltous ions or quinol.

(ii) *Effect on oxidised film.* Films were spread on 0·01*N*-sulphuric acid and allowed to oxidise to either the unstable (XO_2') or the stable (XO_2) peroxide. The potential was then measured before and after injecting either cobaltous ions or quinol into the substrate, with the following results:

Effect of Quinol on Dipole Moment of Oxidised Film.

Film.	Temp.	Concn. of quinol, %.	μ (in Debye units) at A = 330 A.²/mol. Before injection.	After injection.	Diff. on injection.
XO_2'	18°	0·02	2·52	2·38	− 0·14
XO_2'	18	0·10	2·43	2·29	− 0·14
XO_2'	18	0·10	2·53	2·43	− 0·10
XO_2	30	0·10	2·65	2·54	− 0·11
XO_2	38	0·10	2·54	2·38	− 0·16
				Mean =	− 0·13

Effect of Cobaltous Ion on Dipole Moment of XO_2 *Film.*

Temp.	Concn. of $Co^{\cdot\cdot}$, %.	μ (in Debye units) at $F = 1$. Before injection.	After injection.	Diff. on injection.
36°	0·005	2·44	2·20	− 0·24
35	0·005	2·50	2·30	− 0·20
			Mean =	− 0·22

The mean decreases in μ of 0·13 and 0·22D are approximately equivalent to 15 and 22 millivolts, respectively.

The results of the experiments are in accord with expectations, and it is of interest to note further that injection of cobaltous ions under a polymerised film produced no change of potential, and of course no complex formation could be anticipated in this case.

Experiments were then carried out with films containing various proportions of the following esters:

(1) Ethyl myristate, $CH_3{\cdot}[CH_2]_{12}{\cdot}CO_2C_2H_5$.
(2) Methyl linoleate, $CH_3{\cdot}[CH_2]_4{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CH{:}CH{\cdot}[CH_2]_7{\cdot}CO_2CH_3$.
(3) Ethyl linolenate, $C_2H_5{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CH{:}CH{\cdot}CH_2{\cdot}CH{:}CH{\cdot}[CH_2]_7{\cdot}CO_2C_2H_5$.
(4) Methyl β-elæostearate, $CH_3{\cdot}[CH_2]_3{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}CH{:}CH{\cdot}[CH_2]_7{\cdot}CO_2CH_3$.

For the last three esters we are indebted to Imperial Chemical Industries, Ltd. (Dyestuffs Group).

In view of the unsaturated nature of three of these esters it was of interest to examine the stability of the films, as we might expect to find autoxidation proceeding at a measurable rate. Experiments showed that films of methyl linoleate and ethyl linolenate are stable on 0·01*N*-sulphuric acid at room temperature, but that methyl β-elæostearate shows a slow rise of ΔV on standing. Films of all three esters spread on 0·01*N*-sulphuric acid + 0·003% potassium permanganate gave potentials which were initially higher than on the acid alone but fell rapidly, presumably owing to disruptive oxidation. If the permanganate concentration was reduced to 0·0001% some indications of an initial rise of potential were observable, this being followed as before by a steady fall. Some films were also spread on 0·01*N*-

sulphuric acid + 5×10^{-4} *M*-cobalt sulphate, the results being similar to those on the acid alone except that the oxidation of the methyl β-elæostearate was accelerated. A few experiments were carried out on this substrate to determine the effect of pressure on the oxidation process. The reaction was followed by measuring the surface potential, and was found to obey an approximate pseudo-bimolecular law. The results show that the oxidation velocity is independent of the compression for areas greater than 80 A.^{2}/molecule, but falls rapidly at higher compression; the transition is in good agreement with the area at which the pressure begins to rise rapidly. The reaction thus seems to be essentially similar to the autoxidation of maleic anhydride β-elæostearin (*loc. cit.*).

Reactions in Mixed Films.—We now consider the effects produced by diluting films of maleic anhydride β-elæostearin with various proportions of these esters, and we require to know first how the area and phase-boundary potential of the mixed film are related to the values for the separate components. The simplest assumption—that the areas and moments of the constituents of a mixture are additive—has been shown by Schulman and Hughes (*Biochem. J.*, 1935, **29**, 1243) to be of limited validity. In this particular case the agreement with the simple law of addition found experimentally is in general satisfactory, although ethyl myristate when present in large concentrations shows a tendency to expand the film. It is assumed, further, that the polymer also occupies the same area per molecule and has the same dipole moment in mixed films as when present alone. This cannot readily be tested directly, but it is noted that the areas found do not decrease so markedly as one would expect as the polymer size is decreased by increasing the ester concentration (see below). For the purpose of studying the reaction velocity it is immaterial whether this condition is fulfilled, provided that the observed area gives a linear measure of the extent of reaction: this is assumed to be the case.

Preliminary experiments (*Trans. Faraday Soc.*, 1936, **32**, 187) showed that none of the esters has any effect on the rate of oxidation, but that all retard the polymerisation. The four esters were chosen to form a series of varying degrees of unsaturation, as it was anticipated that the inhibitory efficiency would decrease with increasing unsaturation. The quantitative study of the effect of esters on the polymerisation velocity is based on the use of the " Semenoff " constant, employed in the study of the kinetics of the process of polymerisation (*Proc. Roy. Soc.*, 1935, *A*, **153**, 116, 129), and observations have also been made of the symmetry of the velocity curves. If A_0, A_∞, A_m are respectively the areas at the start of the reaction, at the end, and at the point of maximum velocity, we define a symmetry function ρ by the equation

$$\rho = (A_m - A_0)/(A_\infty - A_0) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

An analysis of the kinetics of polymerisation chain reactions (*Trans. Faraday Soc.*, 1936, **32**, 656; for a note on its application to polymerisation in monolayers, see also *Proc. Roy. Soc.*, 1936, *A*, **155**, 692) shows the importance of this quantity in elucidating the mechanism of polymerisation, and also leads to the conclusion that the effect of inhibitors would in bulk phase normally be to decrease ρ. In film polymerisation we have to take into account another factor. It has been shown (*Trans. Faraday Soc.*, 1936, **32**, 666) that deactivation by an inhibitor leads to a progressive decrease in the mean chain length of the polymer during the reaction, especially during the later stages (*ibid.*, pp. 656, 666). This means that towards the end of the polymerisation only very short-chain products are being produced, and these will have comparatively little effect on the area, so that the final area attained will be reduced to a much greater extent than will the area corresponding to the maximum velocity. This factor will clearly increase ρ, so it is impossible to predict qualitatively the net variation of ρ. It is important to note that this phenomenon would not be nearly so marked if the parameter employed in following the polymerisation were proportional to N, the total number of molecules present, since $N_\infty/N_0 = 1/\nu_\infty$ which is in any case small (ν = mean chain length of polymer), and $(1 - N_\infty/N_0)$ will not therefore vary significantly with ν_∞ unless this becomes very small. In our case we have taken $(A_\infty - A_0)$ to be a measure of ν_∞ (*Proc. Roy. Soc.*, 1935, *A*, **153**, 140).

Turning now to consider the effect of the esters on the reaction rate, we require to find some way of obtaining a quantitative measure of the inhibitory efficiencies of the various esters. Empirically the velocity constant (k) of an inhibited chain reaction is related to the constant (k_0) with no inhibitor and the concentration (c) of inhibitor by the equation (Jeu and Alyea, *J. Amer. Chem. Soc.*, 1933, **55**, 575):

$$k = k_0/(1 + pc) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

where p is a specific constant for the inhibitor.

A complete kinetic analysis of the problem has proved mathematically intractable, but it has been shown (*Trans. Faraday Soc.*, 1936, **32**, 666) that for two simple cases of inhibition Jeu and Alyea's method (*loc. cit.*) gives a reasonably good approximation. These authors re-write the empirical equation (2) in the form:

$$k = k_1k_2/(k_3 + k_4c) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where k_1, k_2, k_3, and k_4 are respectively the velocity constants for the initiation, propagation, termination (spontaneous), and termination (by inhibitor) of the chain; also, they identify the chain length as

$$\nu = k_2/(k_3 + k_4c) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Now these formulæ are only true for *long* chains; for short chains the initial activation is not negligible, and we must write

$$k = k_1[1 + k_2/(k_3 + k_4c)] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

and

$$\nu = k/k_1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (6)$$

From (5)

$$k_0 = k_1(1 + k_2/k_3) \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

Now experimentally k_0 is found to vary, not only with different samples of material, but also during the course of a day's experiments, a gradual decrease of k_0 being frequently observed, probably due to variations in k_3, the rate of 'spontaneous' deactivation, *e.g.*, by the presence of adventitious impurities which act as inhibitors. By eliminating k_3 between (5) and (7) we find

$$\frac{k}{k_0 - k} = k_1\left\{\frac{1}{k_0 - k_1} + \frac{k_0}{(k_0 - k_1)^2pc}\right\} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (8)$$

where

$$p = k_4/k_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

and may be termed the coefficient of inhibition. If we denote $(k_0/k - 1)$ by x, equation (8) gives us $1/x$ for any observed k_0 and for any values of k_1 and p. We may define the total error E as

$$E = \Sigma(x_{\text{obs.}} - x_{\text{calc.}})^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (10)$$

where the summation extends over all the experiments with a single ester. We now require to find those values of k_1 and p which make E a minimum, and the most direct way would be to solve the equations

$$\partial E/\partial k_1 = \partial E/\partial p = 0 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

In view of the cumbersome form of expression involved, it is simpler and less laborious to proceed as follows: if we assume a value for k_1, p can be calculated from each experiment, and it is then a simple matter to find the value of p which gives the minimum value of E for the assumed k_1. By proceeding in this way, E can be plotted as a function of k_1, the minimum of the curve giving the required value of k_1, and thence of p. This method of analysis has been applied to all the suitable data available, the results being summarised below.

The first figures to be considered were those for the polymerisation of XO_2 in mixtures containing ethyl myristate or methyl β-elæostearate at $F = 12$ and 35°, the following results being obtained:

Experimental Application of Equation (8).

k_1 (min.$^{-1}$).	Ethyl myristate. p.	E.	Methyl β-elæostearate. p.	E.	p_1/p_2.
0·08	2·1	0·0445	—	—	—
0·09	3·3	0·035	0·85	0·109	3·9
0·095	3·8	0·029	—	—	—
0·10	4·5	0·029	1·1	0·097	4·0
0·11	6·2	0·034	1·35	0·097	4·6
0·12	—	—	1·7	0·114	—
k for $E_{min.}$ (min.$^{-1}$)	0·098		0·105		

k_1 should, of course, be independent of the ester, and the agreement found between the two series is highly satisfactory; $k_1 = 0{\cdot}10$ has been taken as the final result, and p values calculated for the other esters by using this figure. (The data were too scanty to justify separate calculations of k_1.) We may note from this table that ratios of p will not be seriously affected by a small error in k_1.

The final figures obtained for the inhibitory efficiencies of the esters in the polymerisation of XO_2 are given in the following table, which includes also results at a higher temperature.

Inhibitory Efficiencies of Esters.

Ester.	Results at $F = 12$; 35° ($k_1 = 0{\cdot}10$ min.$^{-1}$). No. of expts.	p.	Ratio of p's.	Results at $F = 12$; 40° ($k_1 = 0{\cdot}15$ min.$^{-1}$). No. of expts.	p.	Ratio of p's.	Weighted mean ratio.
Ethyl myristate	6	4·5	(1·0)	2	3·15	(1·0)	(1·0)
Methyl linoleate	2	1·8	0·40	1	1·0	0·32	0·37
Ethyl linolenate	4	1·3	0·29	1	1·15	0·37	0·31
Methyl β-elæostearate	7	1·1	0·24	—	—	—	0·24

The inhibitory efficiencies are in the direction anticipated. Employing these values of p and k_1, we have calculated velocity constants by means of equation (8) for the polymerisation of XO_2 at $F = 12$ and 35° for mixtures containing ethyl myristate or methyl β-elæostearate, and these are compared below with the experimental values:

Polymerisation Velocity Constants in Mixed Films.

Ethyl myristate. k_0 (min.$^{-1}$).	C (%).	k (min.$^{-1}$), obs.	calc.	Methyl β-elæostearate. k_0 (min.$^{-1}$).	C (%).	k (min.$^{-1}$), obs.	calc.
0·355	5	0·256	0·258	0·324	5	0·257	0·275
0·315	10	0·213	0·203	0·304	10	0·224	0·246
0·322	15	0·172	0·179	0·272	15	0·214	0·187
0·290	25	0·159	0·150	0·408	25	0·269	0·252
0·230	25	0·143	0·144	0·260	25	0·186	0·201
0·219	25	0·137	0·143	0·254	25	0·217	0·198
				0·240	25	0·183	0·193

The better agreement found for ethyl myristate is to be anticipated, in view of its much larger inhibitory efficiency. The small temperature range employed does not justify any discussion of the temperature coefficient of either k_1 or p.

Three series of experiments on the polymerisation of the unstable peroxide in mixed films gave no consistent results, the experimental difficulties being too great.

An interesting case of polymerisation in mixed films is that of the polymerisation of XO_2' in the presence of XO_2, the conditions being such that the latter does not polymerise at an appreciable rate (*Proc. Roy. Soc.*, 1935, *A*, **153**, 116, 129). Two series of experiments of this type have been analysed, for polymerisation at (i) $F = 8$ and 22°, (ii) $F = 10$ and 17°, the values of k_0, k_1, and p being as follows:

Polymerisation of XO_2' *in presence of* XO_2.

Temp.	F (dynes/cm.).	k_0 (extrap.).	k_1.	p.	v_∞ (= k_0/k_1).
22°	8	6·65	0·82	1·4	8·1
17	10	0·107	0·022	0·7	4·9

We may now employ the data collected above to make an estimate of the chain lengths of the polymers produced under various conditions, by means of equation (6). Although the results of this process can make no claim to precision, yet they do indicate the order of polymer size. In the penultimate table the chain length is given by $\nu_\infty = 10k$, so that the product of the uninhibited polymerisation of XO_2 has a chain length of the order $2 \sim 4$. A difficulty arises in the case of the inhibited reactions from the fact that the chain lengths of some of the "polymers" prove to be less than 2. It is probable therefore that the values of ν estimated by this method are correct only as to order of magnitude, a conclusion we have already anticipated.

SUMMARY.

The mechanism of positive and negative catalysis of polymerisation by cobalt and quinol respectively is examined by the phase-boundary potential method. It is concluded that positive polymerisation catalysis involves the formation of a complex with the catalyst, whereas oxidation catalysis does not require this mechanism.

The stability of films of the following esters is examined: Ethyl myristate, methyl linoleate, ethyl linolenate, methyl β-elæostearate. Of these only the last undergoes autoxidation at an appreciable rate when spread as a monolayer on 0·01*N*-sulphuric acid.

Experiments in which films of maleic anhydride β-elæostearin were diluted with one of the above esters are discussed. The oxidation rate remains unchanged, but the polymerisation is retarded. A semi-quantitative study of this inhibition is presented which shows that the inhibitory efficiency of the esters decreases with increasing unsaturation. An estimate of the polymer chain lengths based on this analysis suggests that the mean polymer size rarely if ever exceeds 10 units and is probably usually <5.

One of us (G. G.) desires to thank Imperial Chemical Industries, Ltd. (Dyestuffs Group), for financial aid.

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157. *Hydrogen Cyanide Synthesis of Aromatic Aldehydes. Part I. Dibenzfuran-3-aldehyde.*

By L. E. HINKEL, E. E. AYLING, and J. H. BEYNON.

NOT only phenols and phenolic ethers (compare Gattermann, *Annalen*, 1907, **357**, 313) but also many aromatic hydrocarbons lend themselves to the hydrogen cyanide aldehyde synthesis (J., **1936**, 339). It has now been found that, in general, the introduction of substituents other than chlorine (J., 1936, 342), hydroxyl or alkoxyl tends partly or completely to inhibit aldehyde formation. For instance, the following compounds, when subjected to the reaction, are either recovered unchanged, or in several cases, converted into resin-like solids: nitrobenzene, *o*-nitrophenol, benzoic and cinnamic acids, aniline, diphenylamine and dimethylaniline, azobenzene, benzophenone, anthraquinone and 1 : 5-dihydroxyanthraquinone. Although phenol and diphenyl readily yield aldehydes, yet, contrary to expectation, 2-hydroxydiphenyl, 2-methoxydiphenyl and 2 : 2′-dihydroxydiphenyl do not. In the last case, the aluminium chloride causes the removal of a molecule of water, resulting in an almost quantitative conversion into dibenzfuran (diphenylene-oxide). The isolation of this compound, however, suggested that the introduction of the ethereal oxygen bridge into diphenyl should, at any rate, not inhibit the introduction of the aldehyde group. This expectation has been realised and the reactions of the resulting aldehyde have been investigated.

The aldehyde group in dibenzfuranaldehyde occupies position 3 (para to the oxygen link), since oxidation yields dibenzfuran-3-carboxylic acid, m. p. 247° (Mayer and Krieger, *Ber.*, 1922, **55**, 1659). *Dibenzfuran-3-aldehyde* displays the characteristic properties of aromatic aldehydes and readily undergoes the benzoin condensation, the corresponding benzil and benzilic acid thence being obtained in the usual manner.

When the aldehyde is subjected to the Perkin reaction, the corresponding *acrylic acid* is obtained, which yields very sparingly soluble salts with alkalis, the ammonium salt being the most and the sodium salt the least soluble in water. The aldehyde also condenses with malonic acid, yielding a dibasic acid which on heating is converted into the same acrylic acid.

With dimethylaniline, condensation proceeds normally to yield a leuco-base, which is readily oxidised to an intense green dye of the malachite-green series.

EXPERIMENTAL.

Preparation of Dibenzfuran-3-aldehyde.—The procedure was that described by Hinkel, Ayling, and Beynon for the general preparation of aldehydes (J., 1936, 341). Dibenzfuran (21 g., 1 mol.), tetrachloroethane (80 c.c.), hydrogen cyanide (15 c.c., 3 mols.), and aluminium chloride (42 g., 2·5 mols.) were allowed to react in presence of a stream of hydrogen chloride for 5 hours at 80°. The dark viscous mixture was poured on ice and concentrated hydrochloric acid and boiled for a few minutes, and the solvent distilled in steam; the residual oil solidified on cooling. The solid was extracted with ether, the ethereal solution shaken for 8 hours with excess of saturated aqueous sodium bisulphite, and the light brown bisulphite compound removed, washed with ether, and boiled for 5 minutes with dilute sulphuric acid. The oil obtained solidified on cooling and crystallisation from light petroleum (b. p. 80—100°) yielded *dibenzfuran-3-aldehyde* (21 g.; 81%) in colourless laminæ, m. p. 68° (Found: C, 79·0; H, 4·2. $C_{13}H_8O_2$ requires C, 79·6; H, 4·1%). The aldehyde readily yielded the following derivatives by the usual methods: the *phenylhydrazone*, pale yellow plates, m. p. 162°, from alcohol (Found: N, 9·8. $C_{19}H_{14}ON_2$ requires N, 9·8%); the *aniline* derivative, pale yellow needles, m. p. 131°, from light petroleum (b. p. 80—100°) (Found: N, 5·1. $C_{19}H_{13}ON$ requires N, 5·2%); the *semicarbazone*, colourless plates, m. p. 240°, from alcohol (Found: N, 16·5. $C_{14}H_{11}O_2N_3$ requires N, 16·6%); and the *oxime*, colourless laminæ, m. p. 129°, from light petroleum (b. p. 80—100°) (Found: N, 6·6. $C_{13}H_9O_2N$ requires N, 6·6%).

Oxidation of Dibenzfuran-3-aldehyde.—The aldehyde (1·0 g.), suspended in 4*N*-sodium hydroxide (1 c.c.), was boiled with a solution of potassium permanganate (1·2 g.) in water (100 c.c.) until the colour had disappeared. The filtered liquid, on acidification with concentrated hydrochloric acid, yielded a white precipitate, which was washed with water and crystallised from aqueous alcohol, dibenzfuran-3-carboxylic acid (0·7 g.) separating in colourless needles, m. p. 247° after slight softening at 237° (Found: equiv., 212. Calc., 212) (Mayer and Kreiger, *loc. cit.*, record m. p. 246—247°, and name it diphenyleneoxide-5-carboxylic acid on their system of ring numbering).

Benzoin Condensation of Dibenzfuran-3-aldehyde.—The aldehyde (4 g.) was boiled under reflux for 3 hours with a solution of potassium cyanide (0·45 g.) in alcohol (15 c.c.) and water (5 c.c.), and the resulting mixture poured into water (20 c.c.); an oily layer then separated. This, on crystallisation from benzene–light petroleum (b. p. 80—100°), yielded *3-dibenzfuroyl-3-dibenzfurylcarbinol*, $C_{12}H_7O{\cdot}CO{\cdot}CH(OH){\cdot}C_{12}H_7O$, in very pale yellow, stellate clusters (3 g.), m. p. 130° (Found: C, 79·5; H, 4·1. $C_{26}H_{16}O_4$ requires C, 79·6; H, 4·1%).

Oxidation of the Carbinol.—The carbinol (2 g.) and nitric acid (*d* 1·42, 1·7 c.c.) were heated at 100° for 2 hours, and the resulting brown solid washed with water. *Bis-3-dibenzfuryl diketone* (1·8 g.) crystallised from alcohol in microscopic yellow needles, m. p. 236—237° (Found: C, 79·9; H, 3·65. $C_{26}H_{14}O_4$ requires C, 80·0; H, 3·6%).

"Benzilic Acid" Transformation.—The diketone (2 g.) and potassium hydroxide (1·2 g.) were heated with water (3 c.c.) and alcohol (14 c.c.) for 10 minutes at 100°, the mixture poured into water (100 c.c.), and the filtered liquid acidified with concentrated hydrochloric acid. The precipitate, crystallised from aqueous alcohol, gave *bis-3-dibenzfurylglycollic acid* (2 g.) in pale yellow, microscopic needles, m. p. 248° (Found: C, 76·6; H, 3·9. $C_{26}H_{16}O_5$ requires C, 76·5; H, 3·9%).

β-Dibenzfuran-3-acrylic Acid.—Dibenzfuran-3-aldehyde (5 g.) was boiled under reflux with fused sodium acetate (4 g.) and acetic anhydride (25 c.c.) for 8 hours and the mixture was poured into water (200 c.c.) and warmed with an excess of sodium carbonate. The brown product, crystallised from toluene, yielded *β-dibenzfuran-3-acrylic acid* (6 g.) in colourless needles, m. p. 239—240° (Found: C, 75·6; H, 4·2. $C_{15}H_{10}O_3$ requires C, 75·6; H, 4·2%), almost insoluble in sodium carbonate and sodium hydroxide but more soluble in potassium hydroxide and ammonia solutions. The *methyl* ester, prepared by heating the acid (1·2 g.) with hydrogen chloride in methyl alcohol (60 c.c.), crystallised from aqueous alcohol in colourless plates, m. p. 130° (Found: C, 76·1; H, 4·7. $C_{16}H_{12}O_3$ requires C, 76·2; H, 4·8%).

Dibenzfuryl-3-methylenemalonic Acid.—Dibenzfuran-3-aldehyde (4 g.), malonic acid (2·1 g.), and glacial acetic acid (2·0 c.c.) were heated at 100° for 3 hours. The solid obtained on cooling was washed with chloroform (20 c.c.) and crystallised from aqueous alcohol, *dibenzfuryl-3-methylenemalonic acid* (3 g.) separating in very pale yellow needles, m. p. 213° (decomp.) (Found: C, 67·9; H, 3·5. $C_{16}H_{10}O_5$ requires C, 68·1; H, 3·5%), readily soluble in alkalis, alcohol and acetic acid. The acid lost carbon dioxide rapidly at 213—215° and the residue, crystallised from toluene, yielded β-dibenzfuran-3-acrylic acid, m. p. and mixed m. p. 239—240°.

Condensation of Dibenzfuran-3-aldehyde with Dimethylaniline.—The aldehyde (4 g.), dimethylaniline (25 c.c.), and freshly fused zinc chloride (33 g.) were heated at 100° for 5 hours with frequent stirring. Water (200 c.c.) was added to the dark green, viscous liquid and the removal of the excess of dimethylaniline by distillation in steam left an oil which solidified on cooling. The solid was crystallised from alcohol, in which it was sparingly soluble, and then from alcohol–benzene, yielding the leuco-base, *3-dibenzfuryl-*pp'*-bis(dimethylamino)diphenylmethane* (7 g.), in colourless needles, m. p. 172° (Found: C, 82·7; H, 6·5; N, 6·5. $C_{29}H_{28}ON_2$ requires C, 82·8; H, 6·6; N, 6·6%).

Oxidation of the Leuco-base.—The leuco-base (4 g.) was dissolved in 4*N*-hydrochloric acid (10 c.c.) and water (400 c.c.), dilute acetic acid (1·6 g. in 5 c.c. of water) added, and the solution stirred while a paste of lead peroxide (3 g.) in water was added. After 10 minutes a solution of sodium sulphate crystals (6 g.) in water (20 c.c.) was added, and the well-stirred mixture filtered to remove lead sulphate. The addition of anhydrous zinc chloride (6 g.) in water (50 c.c.) to the green filtrate, followed by saturated aqueous sodium chloride (500 c.c.), resulted in the deposition of the zinc chloride double salt of 3-dibenzfuryl-*pp'*-bis(dimethylamino)-diphenylmethyl chloride in greenish-purple needles (5·1 g.). It was not, however, found possible to obtain the compound sufficiently pure for analysis.

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UNIVERSITY COLLEGE, SWANSEA. [*Received, March 17th*, 1937.]

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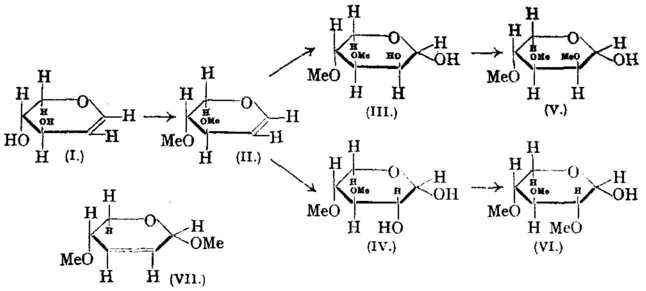
158. *The Ring Structure of Xylal.*

By W. N. HAWORTH, E. L. HIRST, and C. S. WOOLVIN.

IT has been shown previously (Hirst and Woolvin, J., 1931, 1131) that glucal gives on methylation a trimethyl derivative which on treatment with aqueous perbenzoic acid yields 3 : 4 : 6-trimethyl glucopyranose. These observations afforded a direct proof of the pyranose structure of glucal and the present paper is concerned with a similar inquiry into the ring structure of xylal. Methylation of xylal (I) with methyl sulphate and sodium hydroxide gave a syrupy dimethyl derivative which, judging from its physical and chemical properties, consisted almost entirely of *dimethyl xylal* (II). It may have contained, however, a small proportion of the corresponding methylated ψ-xylal (VII) (compare Hirst and Woolvin, *loc. cit.*) and for this reason the physical constants are quoted with reserve.

Dimethyl xylal reacted readily with aqueous perbenzoic acid, giving a mixture of dimethyl xylose (IV) and dimethyl lyxose (III). The behaviour here is normal and is in contrast with that of trimethyl glucal in that under similar conditions the latter substance gave only one of the two expected reaction products, namely, trimethyl glucose, the yield of trimethyl mannose being too small for identification. Further methylation and subsequent hydrolysis of the mixture of methylated pentoses gave rise to a mixture of 2 : 3 : 4-trimethyl xylopyranose (VI) and 2 : 3 : 4-trimethyl lyxopyranose (V), both of which were isolated in the crystalline condition. The isolation of these two sugars in good yield provides a complete proof of the pyranose structure of xylal, since no alteration in ring structure can take place at any stage of the above series of reactions. The presence of trimethyl lyxose in the final product is in itself a guarantee of the structure, since this substance could not in any event be derived from ψ-xylal, because the addition of hydroxyl groups at a double bond by the action of per-acids is known to occur invariably in the *trans*-position.



EXPERIMENTAL.

Dimethyl Xylal.—Diacetyl xylal (14·3 g., prepared by Levene and Mori's method) in acetone (150 c.c.) was simultaneously deacetylated and methylated at 29° by methyl sulphate (41 c.c.) and 30% aqueous sodium hydroxide (101 c.c.). The reagents were added slowly during 2 hours and towards the end the temperature was raised to 40°. In this way decomposition was avoided and the final solution was only slightly yellow (dark coloured products are formed if higher initial temperatures are employed). After a further 90 minutes at 40° the acetone was removed by distillation and the aqueous solution was then shaken with chloroform, which removed the methylated xylal, the latter being obtained as a yellow mobile syrup (4·5 g.) on evaporation of the solvent (Found: OMe, 30%). Methylation was completed by use of Purdie's reagents and on fractional distillation of the product *dimethyl xylal* was obtained as a colourless mobile liquid, b. p. *ca.* 73°/17 mm., $n_D^{20°}$ 1·4566, $[\alpha]_D^{19°}$ − 180° in chloroform (*c*, 0·2) (Found: OMe, 42·4. $C_7H_{12}O_3$ requires OMe, 43·0%. 0·0187 G. of the substance required 0·0203 g. of bromine for saturation of the double bond, corresponding to 98% of the calculated quantity for dimethyl xylal). Dimethyl xylal was very soluble in water and the usual organic solvents.

Action of Perbenzoic Acid on Dimethyl Xylal.—To a solution of dimethyl xylal (4·1 g.) in water (20 c.c.), perbenzoic acid (4·4 g.) in ethereal solution (30 c.c.) was added with cooling. This mixture was shaken at 0° for 5 hours and then kept overnight at room temperature. The aqueous layer was separated and the pale yellow ethereal layer was extracted five times with water. The combined aqueous extracts were neutralised with sodium bicarbonate and the solution was extracted with chloroform. On removal of the solvent the syrupy product was dissolved in ether and after filtration the solution was evaporated again, leaving a colourless syrup (3·7 g.). The latter syrup was dissolved in acetone (40 c.c.) and methylated in the usual way with methyl sulphate (30 c.c.) and 30% aqueous sodium hydroxide (65 c.c.), the temperature being kept low until reducing action disappeared. The product (1·8 g.) was further methylated by silver oxide and methyl iodide and distilled, giving a colourless mobile liquid (1·4 g.), b. p. *ca.* 110°/20 mm., $n_D^{17°}$ 1·4427, $[\alpha]_D$ − 34° in water (*c*, 4·0) (Found: OMe, 57·8. Calc. for $C_9H_{18}O_5$: OMe, 60·2%).

When this distillate (1·37 g.) was heated on the boiling water-bath with 3% hydrochloric acid, the rotation changed in the course of 1 hour from $[\alpha]_D$ − 34° to the constant value + 2° (a mixture containing 57% of trimethyl xylose and 43% of trimethyl lyxose would have $[\alpha]_D$ + 2° in water). The hydrochloric acid was then neutralised by barium carbonate, and the neutral solution evaporated to dryness under diminished pressure. The mixed methylated sugars were extracted with boiling ether and on removal of the ether were obtained as a viscid colourless syrup (1·1 g.). On inoculation with a sample of authentic 2 : 3 : 4-trimethyl lyxose rapid crystallisation ensued and a semi-solid paste was obtained. The syrup (0·8 g.) was drained away on porous tile and the crude trimethyl lyxose (0·30 g., m. p. alone or in admixture with an authentic specimen, 76—77°) was recrystallised from light petroleum, giving characteristic crystals of 2 : 3 : 4-trimethyl lyxose, m. p. alone or when mixed with an authentic specimen of similar m. p., 79°; $[\alpha]_D^{23°}$ − 22° in water (equilibrium value, *c*, 0·9).

The material absorbed in the porous tile was extracted by boiling chloroform and on removal of the solvent was recovered as a stiff colourless syrup. After inoculation with a crystal of

2 : 3 : 4-trimethyl xylose rapid crystallisation took place. After some days the syrupy portion was removed by absorption in porous tile, leaving a hard crystalline mass (0·33 g.), which consisted mainly (80—90%) of 2 : 3 : 4-trimethyl xylose, some 2 : 3 : 4-trimethyl lyxose being present also. Recrystallisation did not effect a separation of the two sugars, but crystallographic measurements, for which we are indebted to Dr. E. G. Cox of this department, established the identity of both and enabled an estimate of their relative proportions to be made. No other crystalline sugar was observed during this examination.

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159. *Degradation of Methylated Inulin to Hexamethyl Difructosan.*

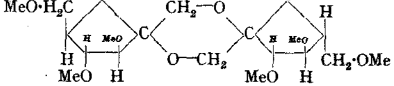
By W. N. HAWORTH, E. L. HIRST, and F. A. ISHERWOOD.

IT is now well established (Haworth, Hirst, and Percival, J., 1932, 2384) that fully methylated inulin has a strong negative rotation ($[\alpha]_D$ − 54°) in chloroform solution. Earlier workers (Irvine and Steele, J., 1920, **117**, 1474) have, however, reported that preparations of methylated inulin may be obtained having positive rotations. Such preparations were made by the use of silver oxide and methyl iodide as methylating agents in the final stages of the work. We have recently encountered an instance in which methylation by this process has altered the rotation of a polysaccharide derivative (Haworth, Hirst, and Waine, J., 1935, 1299) and as the change on this occasion appeared to be connected with disaggregation of the complex unit of the polysaccharide, we wished to gain further insight into the action of silver oxide and methyl iodide on partly methylated polysaccharides. We therefore undertook a detailed examination of the reaction between dimethyl inulin and the Purdie reagents.

It was found that dimethyl inulin ($[\alpha]_D$ − 40°) could be produced either by the method of Irvine, Steele, and Shannon (J., 1922, **121**, 1060) or from inulin acetate by use of an appropriate modification of Haworth and Streight's method (*Helv. Chim. Acta*, 1932, **15**, 609). Further methylation of this substance by silver oxide and methyl iodide under specially drastic conditions invariably gave samples of methylated inulin with strong negative rotations and, beyond a slight change in viscosity the meaning of which in this series is in any case uncertain, no evidence of molecular degradation was observed. Since these experiments had given no indication of the formation of dextrorotatory substances, we proceeded to investigate the possibility of degrading the lævorotatory, fully methylated inulin. We found that boiling the substance for prolonged periods with Purdie's reagents, either in the presence or in the absence of water, had no effect and unchanged methylated inulin was recovered from the reaction mixture.

We succeeded, however, in obtaining a syrup soluble in ether and showing a strong positive rotation ($[\alpha]_D$ + 59°), as the result of heating methylated inulin with methyl iodide containing a little hydrogen iodide. This had properties identical with those given by Irvine, Steele, and Shannon for the dextrorotatory methylated inulin described by them and the analytical figures were those required by a trimethyl inulin. Nevertheless this substance was not a polysaccharide, but had the boiling point and molecular weight of a disaccharide and was, in fact, a hexamethyl difructofuranose 1 : 2-anhydride. We conclude, therefore, that dextrorotatory methylated inulin consisted mainly of this product of depolymerisation.

The reaction is exactly comparable with the similar one in which inulin acetate is depolymerised in chloroform solution by anhydrous nitric acid with formation of hexaacetyl difructofuranose 1 : 2-anhydride in good yield (Irvine and Stevenson, *J. Amer. Chem. Soc.*, 1929, **51**, 2197; Bodycote, Haworth, and Woolvin, J., 1932, 2389). In the present experiments the rotation of different samples of hexamethyl



difructose anhydride varied somewhat, and since three such 1 : 2-anhydrides of fructofur-

anose are stereochemically possible (αα, αβ, and ββ with respect to the glycosidic groups of the fructofuranose units) it would appear that the mode of depolymerisation now under consideration results in the formation of more than one of these possible stereoisomerides.

Similar depolymerisation took place when dimethyl inulin ($[\alpha]_D - 40°$) was heated with methyl iodide containing hydrogen iodide, and the product after methylation was the same as that obtained directly from trimethyl inulin. The structure of the hexamethyl difructose anhydride follows from the observation that it gives on hydrolysis 3 : 4 : 6-trimethyl fructofuranose and from the evidence previously reported (Haworth and Streight, *loc. cit.*).

EXPERIMENTAL.

Partial Methylation of Inulin.—(a) *Simultaneous de-acetylation and methylation of inulin acetate.* Inulin acetate prepared by Haworth and Streight's method (*Helv. Chim. Acta*, 1932, 15, 609) had $[\alpha]_D^{20°} - 33°$ in chloroform (*c*, 1·4), $\eta_{sp.}^{20°}$ in *m*-cresol 0·075 (0·05 g. in 5 c.c.), corresponding to an apparent chain length of 8 fructose units (by the chemical end-group method, 30 units). This acetate (12 g.) was methylated in acetone solution at 35° by the gradual addition of methyl sulphate (50 c.c.) and 30% aqueous sodium hydroxide (140 c.c.) in the usual way. The product, which was insoluble in boiling water, was isolated in the usual manner and obtained by evaporation of its solution in chloroform as a colourless granular solid, $[\alpha]_D^{20°} - 40°$ in chloroform (*c*, 1·0) (Found: OMe, 33·0. Calc. for dimethyl inulin, 32·7%). This material (2 g.) was dissolved in methyl iodide (10 g.) containing just sufficient methyl alcohol to effect solution and then boiled for 8 hours with silver oxide (5 g.). After one treatment the methoxy-content had risen to 38·4% and after a second treatment to 42·9%. The product was a white powder insoluble in ether, $[\alpha]_D^{20°} - 50°$ in chloroform (*c*, 1·0). In this series of experiments no degradation had taken place, but occasionally the product after treatment with Purdie's reagents showed slight acidity and reduced Fehling's solution. This was due to complications arising out of the action of the Purdie reagents on sodium methyl sulphate which contaminated the partly methylated inulin and was never observed when ash-free inulin was used.

(b) *Direct methylation.* Dimethyl inulin, prepared in accordance with the directions of Irvine, Steele, and Shannon (*loc. cit.*), was a crisp white powder, soluble in cold water and chloroform, insoluble in ether. $[\alpha]_{5780}^{20°} - 41°$ in chloroform (*c*, 1·6), $\eta_{sp.}^{20°}$ 0·084 in *m*-cresol (0·05 g. in 5 c.c.), corresponding to an apparent chain length of 8—9 fructose units (Found: OMe, 27·8%). This material was drastically methylated (50 hours' boiling) three times in succession by silver oxide and methyl iodide in the presence of methyl alcohol, the progress of the methylation being shown in the accompanying table.

Substance.	$[\alpha]_D^{20°}$ in chloroform.	$\eta_{sp.}^{20°}$ in *m*-cresol (*c*, 1·0).	OMe, %.
Product after first treatment	− 39°	0·066	31·5
,, ,, second ,, ...	− 40	0·05	35·0
,, ,, third ,, ...	− 43	0·033	38·0

The product after the third treatment was insoluble in boiling ether. Its rotation was only slightly lower than that of the best specimens of methylated inulin of the same methoxyl content and it was obvious that little degradation had been effected. The principal change was in the value of $\eta_{sp.}$. This may indicate some shortening of the chain length, but in view of the insolubility of the product in ether this cannot have been very marked. In this series the viscosity values can be used only for purposes of comparison, since the relationship between viscosity and chain length is highly abnormal.

Degradation of Fully Methylated Inulin. Preparation of Hexamethyl Difructosan.—Since no success had followed the attempts to obtain the supposed dextrorotatory form of methylated inulin by direct methylation of the "dimethyl" derivative, it was decided to investigate its preparation from undegraded fully methylated inulin. Supplies of the last material {$[\alpha]_D^{20°} - 55°$ in chloroform (*c*, 1·03); $\eta_{sp.}^{20°}$ 0·092 in *m*-cresol (*c*, 1·0) (corresponding with an apparent chain length of 9 fructose units); chain length by the chemical end-group method, 30; OMe, 45·4%} were obtained by Haworth, Hirst, and Percival's method (J., 1932, 2384). Degradation of the methylated inulin was attempted in the following ways.

(a) *By boiling with Purdie's reagents in the absence of water.* Methylated inulin (4 g.) was boiled for 16 hours with methyl iodide (20 g., containing a little dry methyl alcohol) and silver oxide (10 g.). The product was extracted with chloroform and on evaporation of the solvent

was obtained as a pale yellow glass, $[\alpha]_D^{20^\circ}$ − 52° in chloroform (*c*, 1·5); $\eta_{sp.}^{20^\circ}$ 0·072 in *m*-cresol (*c*, 1·0). No appreciable degradation took place under these conditions.

(b) *By boiling with Purdie's reagents in the presence of water.* The above experiment was repeated with the addition of 1 c.c. of water to the reaction mixture. The product was a white solid, $[\alpha]_D^{20^\circ}$ − 53°, identical with the material obtained in experiment (a).

(c) *By boiling with methyl iodide containing hydrogen iodide. Preparation of hexamethyl difructosan.* Methylated inulin (10 g.) was boiled for 25 minutes with methyl iodide (50 g. containing a little methyl alcohol) to which hydriodic acid (0·4 c.c.; *d* 1·7) had been added (the methylated inulin dissolved completely in 15 minutes). Silver oxide was then added, and the boiling continued for a short time. The product ($n_D^{19^\circ}$ 1·4680) was isolated in the usual way and distilled, giving: (I) a colourless mobile syrup (2 g.), b. p. 100—140°/0·17 mm., $n_D^{19^\circ}$ 1·4560, $[\alpha]_D^{20^\circ}$ + 30° in chloroform. This material was slightly acid to litmus and reduced Fehling's solution; (II) *hexamethyl difructosan* as a neutral, non-reducing, pale yellow, highly viscid syrup (7·5 g.), b. p. 180°/0·1 mm., $n_D^{18^\circ}$ 1·4702, $[\alpha]_D^{20^\circ}$ + 59·3° in chloroform (*c*, 2·3), *M* 393, 386 (ebullioscopic in benzene). Refractionation through a Widmer column gave only fractions with the same b. p.'s and refractive indices (Found: C, 53·0; H, 8·0; OMe, 45·2. $C_{18}H_{32}O_{10}$ requires C, 52·9; H, 7·8; OMe, 45·6%; *M*, 408). A similar neutral non-reducing viscid product was obtained when the above procedure was applied to " dimethyl inulin." A typical sample of hexamethyl difructosan from dimethyl inulin had b. p. 180°/0·1 mm., $n_D^{16^\circ}$ 1·4730, and $[\alpha]_D^{20^\circ}$ + 38° in chloroform (*c*, 2·3). In different preparations using " dimethyl inulin " as starting material the rotation of the hexamethyl difructosan varied somewhat. Fractions (I) and (II) had properties identical with those of fractions obtained by Irvine, Steele, and Shannon during their work on the methylation of inulin.

Hydrolysis of Hexamethyl Difructosan.—Hexamethyl difructosan (2·85 g.) was hydrolysed by 0·2*N*-sulphuric acid (250 c.c.) at 95°. The reaction was followed polarimetrically: $[\alpha]_D^{20^\circ}$ + 73° (initial value); + 72° (6 minutes); + 66° (63 minutes); + 62° (96 minutes); + 59° (136 minutes); + 56° (178 minutes); + 47·5° (255 minutes); + 42° (326 minutes); + 38·6° (constant value after 600 minutes). The end value corresponds to a value $[\alpha]_D$ + 35·5° for the trimethyl fructose formed during the hydrolysis. That this value is slightly low is accounted for by the observation that furfural derivatives are produced in small quantity during the hydrolysis. From the above figures the value of *k* for the hydrolysis was found to be approximately 0·0035 (minutes and natural logarithms). Jackson and MacDonald (*J. Bur. Standards*, 1931, **6**, 709) report *k* = 0·0083 for the hydrolysis of the difructosan, m. p. 164°. The solution was neutralised with barium carbonate and filtered (charcoal). It was then evaporated to dryness in the presence of a trace of barium carbonate. The product (3 : 4 : 6-trimethyl fructofuranose) was extracted with a warm mixture of alcohol and ether and on removal of the solvent was obtained as a colourless syrup, $n_D^{19^\circ}$ 1·4685, $[\alpha]_D^{20^\circ}$ + 25° in chloroform (*c*, 1·57) (Found: OMe, 41·4. Calc. for $C_9H_{18}O_6$: OMe, 41·9%). Its physical properties are identical with those of 3 : 4 : 6-trimethyl fructofuranose and with phenylhydrazine it gave in 75% yield 3 : 4 : 6-trimethyl glucosazone hydrate, m. p. 80—81°, alone or when mixed with an authentic sample (Found: C, 60·4; H, 7·2; N, 14·0; OMe, 21·8. Calc. for $C_{21}H_{28}O_4N_4$: C, 60·3; H, 7·2; N, 13·4; OMe, 22·2%).

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160. *Polysaccharides. Part XXIV. Yeast Mannan.*

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THE polysaccharide constituents of yeast include glycogen and the so-called " yeast gum," which occurs mainly in the cell wall and was first isolated by Salkowski (*Ber.*, 1894, **27**, 497, 925). It was later recognised as a derivative of mannose and is of special interest on this account, since few of the naturally occurring mannans have so far been the subject of investigation. The mannan of ivory-nut was found by Klages (*Annalen*, 1934, **509**, 159) to consist of a chain of β-mannopyranose units linked through the 1 : 4-positions. It has therefore a structure similar to that of cellulose. In contrast with this the mannan described by Haworth, Raistrick, and Stacey (*Biochem. J.*, 1935, **29**, 612) had a chain-structure in which α-mannopyranose units are linked together through positions 1 and 6. Yeast

mannan, as will appear from the present paper, differs fundamentally in structure from both these and contains a chain of mannose units linked through positions 1 and 6, but with a mannopyranose unit linked glycosidically to the second carbon atom of each alternate mannose unit in the chain. The full implications of this will be discussed when the evidence on which this conclusion is based has been presented.

The yeast mannan was extracted from the cell wall by the action of boiling dilute alkali on baker's yeast. It was separated from other extracted materials in the form of its copper hydroxide complex and after removal of the copper was purified by repeated precipitation from aqueous solution by alcohol. The white powder so obtained was essentially homogeneous and could not be separated into fractions having different properties. It gave only mannose on hydrolysis.

It could be readily acetylated by treatment with pyridine and acetic anhydride and the *acetate* resisted all attempts to separate from it fractions showing different properties. Either from this acetate, by simultaneous de-acetylation and methylation, or by direct methylation of the polysaccharide, the same methylated derivative was obtained. Rigorous fractionation of this material failed to give portions differing materially from one another and it appeared to be essentially homogeneous. This methylated mannan gave solutions of low viscosity compared with similar solutions of methylated starch or methylated cellulose, but in view of the chemical constitution no attempt has been made to apply Staudinger's equation for molecular weight determinations. But the particle weight determined by osmotic pressure measurements (Carter and Record, *J. Soc. Chem. Ind.*, 1936, **55**, No. 11, "Chemistry & Industry," p. 218) is very large (*ca.* 100,000, *i.e.*, 500 mannose units).

Like the original polysaccharide, methylated yeast mannan showed resistance to weak or highly dilute hydrolytic agents, but it was hydrolysed almost quantitatively and without appreciable decomposition by treatment with methyl-alcoholic hydrogen chloride at 150° under pressure. There were three main products, obtained in approximately equimolecular proportions, namely 2 : 3 : 4 : 6-tetramethyl methylmannopyranoside, 2 : 3 : 4-trimethyl methylmannopyranoside, and 3 : 4-dimethyl methylmannopyranoside. Proof of the identity of these substances was obtained in the following ways :

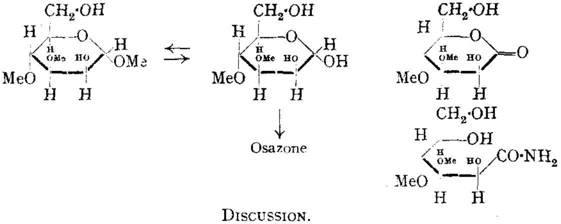
(a) The tetramethyl methylmannoside gave on hydrolysis 2 : 3 : 4 : 6-tetramethyl mannose, recognised both as the sugar and its crystalline anilide and by its transformation by oxidation into the crystalline 2 : 3 : 4 : 6-tetramethyl mannonolactone (Drew, Goodyear, and Haworth, J., 1927, 1243). There can be no doubt, therefore, of the identity of this constituent.

(b) Equally convincing proof of the identity of the trimethyl methylmannoside was obtained by its conversion into the crystalline sugar, from which on oxidation by bromine water the crystalline lactone of 2 : 3 : 4-trimethyl mannonic acid was obtained. Finally the sugar gave on oxidation by nitric acid 2 : 3 : 4-trimethyl mannosaccharic acid. The last substance was formed without loss of a methoxyl group and position 6 must therefore have been a primary alcoholic group. The lactone obtained by oxidation with bromine water was definitely a δ-lactone and it follows immediately that the three methyl groups were severally situated at C_2, C_3, and C_4.

(c) The dimethyl methylmannoside gave on hydrolysis a crystalline dimethyl mannose which, on oxidation by bromine water, gave a crystalline dimethyl mannonolactone and from its rate of hydrolysis in aqueous solution the lactone was identified as belonging to the δ-series. This indicated that a methoxyl group was attached to C_4, since under the conditions adopted for lactonisation of the dimethylmannonic acid it is expected that a γ-lactone would be formed if this mode of lactonisation were possible. Further decisive evidence on this point was provided by a study of the reaction between the free dimethylmannose and cold methyl-alcoholic hydrogen chloride. It is known that in the mannose series formation of a methyl mannofuranoside readily and fairly rapidly takes place under these conditions. In the present instance no evidence of furanoside formation could be observed and no reaction took place until the solution was heated and conditions for pyranoside formation were employed.

One of the methoxyl groups is therefore attached to C_4. The other cannot be at C_6,

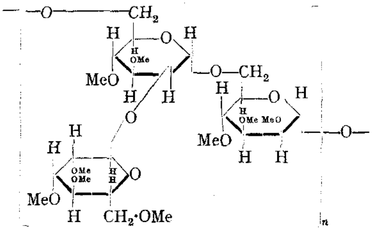
because *4 : 6-dimethyl* mannose is known (Ault, Haworth, and Hirst, *J.*, 1935, 517) and is obviously not identical with the sugar now under discussion. There remains only the choice between C_2 and C_3 and this is easily made in view of the observations that the dimethyl mannose gives an osazone without loss of a methoxyl group and that the amide prepared from the dimethyl mannonolactone gives a strong positive Weerman reaction with sodium hypochlorite. There is, therefore, no methoxyl group at C_2 and the dimethyl sugar must be identified as 3 : *4-dimethyl mannose.*



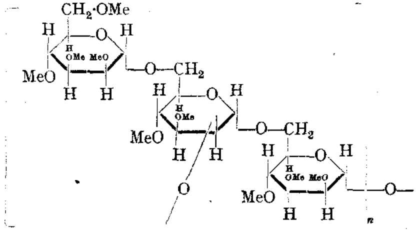
DISCUSSION.

These results show that methylated mannan contains in its structure three types of residues which are united in the polysaccharide molecule. The size of this molecule is unknown but it is probably large. In any possible structural formulæ the following conditions must be satisfied: (a) one in every three of the mannose residues must be

(I.)



(II.)



attached by its reducing group to another mannose residue and must form a terminated side chain, (b) one in every three of the mannose residues is attached at positions C_1 and C_6 to other residues, and (c) the third mannose residue is attached to other mannose residues at positions C_1, C_2, and C_6.

Two types of structure will satisfy these conditions and these are represented in their simplest form in (I) and (II).

The formula (I) comprises a chain of α-mannopyranose units linked through the 1 : 6-positions with a mannose unit joined at C_2 of every alternate residue. The formula (II) postulates a chain of mannopyranose units joined alternately by 1 : 6 and 1 : 2 links, but at the 6-position of the latter unit a further mannopyranose residue is attached through its reducing group. There are at present no polysaccharides of this type of structure known, but on the present evidence such a constitution cannot be excluded. For each bracketed structure where $n = 1$ in formulation (II) a trisaccharide anhydride is represented, but the minimum molecular weight determined by the Rast method rules out the possibility at once and the properties of the methylated mannan indicate that n is probably a large number. Since n is greater than unity, various possibilities present themselves. (a) The molecule may exist as a large ring. (b) The molecule may be a terminated chain and in this case it is to be remarked that a terminated chain would reveal itself on hydrolysis, not necessarily by the presence of additional tetramethyl mannose but by the presence of a molecule of 3 : 4 : 6-trimethyl mannose (I) or 2 : 3 : 4-trimethyl mannose (II). Beyond the fact that the observed amount of trimethyl mannose is slightly greater than that of the tetramethyl derivative, nothing can be said on this point at the moment. The search for a small amount of 3 : 4 : 6-trimethyl mannose in an excess of 2 : 3 : 4-trimethyl mannose is not an easy problem to solve. (c) The molecule may be essentially as described under (b), but aggregation to larger units, comprising some 500 mannose residues, may occur by one or other of the mechanisms suggested by Haworth, Hirst, and Oliver (J., 1934, 1917) as applicable to xylan, starch, and other polysaccharides.

Although the formula (I) shows the 1 : 6-union of adjoining mannopyranose groups as α, this stereochemical arrangement is based only on the high dextrorotation of the mannan and on the fall in rotation on complete hydrolysis. This does not exclude the possibility of the presence of some β-linkages.

Experimental.

Preparation of Yeast Mannan.—Baker's yeast (7 kg.) was boiled for 8 hours with 6% sodium hydroxide solution (15 l.). The solution was centrifuged, and the clear liquid concentrated under diminished pressure to 3·5 l. After acidification by addition of acetic acid sodium nucleate was deposited as a slime. The solution was then centrifuged and separated into three layers: (a) a sticky solid in the upper portion of the tubes, (b) a clear liquid, (c) a granular precipitate collected on the bottom of the tubes. (a) and (c) were combined, stirred with dilute acetic acid, and centrifuged again. The clear liquid from this operation was combined with (b), filtered through glass wool, neutralised with sodium hydroxide, and concentrated to 1 l. Addition of alcohol (to make the final concentration of alcohol 65%) precipitated crude mannan, which was separated and washed with 60% alcohol. It was dissolved in water (800 c.c.), the solution adjusted until it was only slightly alkaline, and Fehling's solution was added until the colour of the liquid above the grey-blue precipitate was deep blue. The precipitate was thoroughly washed with warm water, then suspended in water (1 l.), and concentrated hydrochloric acid was slowly added with stirring, the solution being kept greenish-grey in colour. When all the mannan–copper complex had dissolved, a little more acid was added and the solution was poured into alcohol (3 vols.). The precipitate, after being washed with alcohol, was dissolved in water and reprecipitated with alcohol (this precipitation proceeds best if the aqueous solution is slightly acid). The precipitate was then dissolved in water (1 l.) and the solution, rendered just alkaline by potassium hydroxide, was poured into alcohol (3 l.). The precipitate of crude mannan was washed with alcohol and dried at 50° under diminished pressure. Yield, 150 g. $[\alpha]_D^{20^\circ} + 73°$ in water (c, 1·0).

The crude mannan (400 g., collected by repetitions of the above procedure) was dissolved in warm water (2·5 l.). Glacial acetic acid (750 c.c.) was then added and the solution was treated with charcoal, filtered, and poured slowly into methylated spirit (10 l.). The precipitate was collected, and the procedure repeated twice. The *mannan* (260 g.) obtained after the third precipitation had the following properties: white hygroscopic powder, readily soluble in cold water; no colour with iodine in aqueous solution; iodine number negligible; non-reducing to Fehling's solution. On titration with sodium hydroxide the amount of alkali used was negligible; when the mannan was boiled with 12% hydrochloric acid, the amount of furfural liberated was negligible (absence of pentose sugars and uronic acids); $[\alpha]_D^{24^\circ} + 89°$ in water (c, 1·4) [Found: C, 44·5; H, 6·1; N, nil. $(C_6H_{10}O_5)_n$ requires C, 44·4; H, 6·2%].

Fractional precipitation of yeast mannan from aqueous solution by gradual addition of alcohol gave a series of fractions with properties identical with those just described. Hydrolysis of yeast mannan with fuming hydrochloric acid in the cold was unsatisfactory. Better results were obtained by hydrolysis with 2*N*-sulphuric acid at 95°. In the course of 5 hours the rotation fell regularly from $[\alpha]_D$ + 80° to the constant value + 12° (for mannose the value of $[\alpha]_D$ is + 15°). The final solution was dark and some decomposition had taken place. After neutralisation with barium carbonate and treatment with charcoal, the solution was evaporated to a syrup (diminished pressure). This syrup slowly crystallised. After some days the syrupy portion was washed away by 50% acetic acid, leaving crystalline mannose (m. p. 131°; $[\alpha]_D^{20°}$ + 15°, equilibrium value in water, *c*, 3·0; yield, 25% of the theoretical). On addition of phenylhydrazine to the acetic acid solution of the syrup a copious precipitate of mannose phenylhydrazone was obtained (yield, 50% of the theoretical). Control experiments in which mannose was subjected to exactly the above procedure showed that the recovery of mannose amounted to 82% of the theoretical. Using this correction, we find that in the hydrolysis of mannan a minimum yield of 92% of the theoretical quantity of mannose was obtained. It may be concluded, therefore, that in all probability yeast mannan is composed entirely of mannose residues.

Acetylation of Yeast Mannan.—(a) Mannan (15 g.) was dissolved in warm water (100 c.c.) and alcohol (900 c.c.) was added slowly to the solution. The precipitated mannan was separated and immediately acetylated by acetic anhydride (150 c.c.) and pyridine (200 c.c.). The mixture was kept at 80° for 30 hours with stirring. Nearly all the mannan dissolved and the small residue was filtered off. The solution was poured into water, and the *acetate* isolated in the usual way. It was a white powder soluble in acetone, chloroform and hot methyl alcohol, insoluble in water and in cold alcohol. $[\alpha]_D^{24°}$ + 62° in chloroform (*c*, 1·7). $\eta_{sp.}^{20°}$ 0·25 in *m*-cresol (0·05 g. in 5 c.c.). Yield, 85% of the theoretical (Found: $CH_3 \cdot CO$, 45·1. $C_{12}H_{16}O_8$ requires $CH_3 \cdot CO$, 44·8%).

(b) Mannan (10 g.) was treated in exactly the same way and acetylated by a mixture of acetic acid (65 c.c.) containing a little chlorine and acetic anhydride (100 c.c.) containing sulphur dioxide. Acetylation was complete in 2 hours at 65°. The acetate (yield, 70% of the theoretical) had properties the same as those described under (a) except that it had a greater solubility in chloroform and showed a smaller viscosity in *m*-cresol ($\eta_{sp.}^{20°}$ 0·12; 0·05 g. in 5 c.c.).

Mannan acetate [200 g., prepared by the method (a) involving the use of pyridine and acetic anhydride] was carefully fractionated by the gradual addition of light petroleum to a chloroform solution. The data recorded in the accompanying table show that no serious differences are observable in the properties of the fractions, except that the small fraction I contained most of the mineral impurities and is not comparable with the others.

Fraction.	Wt., g.	Ash, %.	$[\alpha]_D^{20°}$ (in $CHCl_3$).	$\eta_{sp.}^{20°}$.*	$CH_3 \cdot CO$, %.
1	12	0·6	+ 52°	0·56	44·4
2	115	0·15	+ 61	0·28	44·6
3	54	0·10	+ 60	0·23	44·0
4	17	0·04	+ 61	0·17	44·6

* 0·05 G. in 5 c.c. of *m*-cresol. The meaning of the viscosity figures is not clear: they appear to be connected closely with the ash content and their possible interpretation in terms of chain length is deferred until further data are available.

Methylation of Yeast Mannan.—(a) Fractions 2 and 3 of the acetate were combined and used for methylation. The acetate (10 g.) in acetone (200 c.c.) was simultaneously de-acetylated and methylated at 55° by the gradual addition during 2 hours of sodium hydroxide (320 c.c., 30% solution) and methyl sulphate (120 c.c.). When all the reagents had been added, the mixture was heated at 100° for 30 minutes. Usually the methylated mannan separated from the hot solution and was filtered off. Occasionally it separated as an emulsion. In such cases the solution was then brought almost to neutrality by addition of sulphuric acid and concentrated, alcohol added to precipitate most of the sodium sulphate, the aqueous alcoholic solution evaporated to dryness, and the residue treated again with methyl sulphate and sodium hydroxide in the presence of acetone. After 8 successive methylations the crude methylated mannan was dissolved in chloroform, the solution was filtered to remove mineral impurities, and after evaporation of the solvent the methylated mannan was dissolved in ether containing a little acetone. Addition of excess of light petroleum threw down methylated yeast mannan as a pale yellow, amorphous powder (yield, 70% of the theoretical), soluble in acetone, chloroform, and

methyl alcohol, insoluble in light petroleum. $[\alpha]_D^{24^\circ}$ + 85° in chloroform (*c*, 1·96); + 84° in methyl alcohol (*c*, 1·5) (Found : OMe, 43·6%).

(b) Methylated mannan is obtainable also by direct methylation in aqueous solution. Mannan (16 g.) in water (100 c.c.) was treated in the usual way at 50° with methyl sulphate (200 c.c.) and sodium hydroxide (400 c.c., 30% solution). When the solution was heated at 100° at the end of the reaction, methylated mannan separated. After 4 methylations (of which 2 were conducted in the presence of acetone) a product identical with that described above was obtained. $[\alpha]_D^{20^\circ}$ + 85° in chloroform (*c*, 1·2); $\eta_{sp.}^{20^\circ}$ 0·08 in *m*-cresol (0·02 g. in 5 c.c.) (yield, 92% of the theoretical) (Found : OMe, 43·5%).

Fractionation of Methylated Yeast Mannan.—Methylated mannan [46 g., prepared by method (a)] was dissolved in a mixture of ether (350 c.c.) and acetone (110 c.c.) and to the solution light petroleum was slowly added, the following fractions (which differed inappreciably from one another) being obtained :

Fraction.	Wt., g.	$[\alpha]_D^{25^\circ}$ (in $CHCl_3$).	$\eta_{sp.}^{20^\circ}$.*	OMe, %.
1	27	+ 89°	0·26	44·1
2	12	+ 86	0·25	43·8
3	7	+ 86	0·19	43·8

* In *m*-cresol (0·05 g. in 5 c.c.).

Molecular weight estimations (fraction 2) by Rast's method in camphor indicated a minimum molecular weight of 3000. The real particle weight may however be very much greater than this.

Hydrolysis of Methylated Yeast Mannan.—After many trial experiments had been carried out it was found that the method of hydrolysis most suitable for the present investigation consisted in heating methylated mannan (21·1 g.) in 1% methyl-alcoholic hydrogen chloride (800 c.c.) at 150° under pressure for 20 hours. Hydrolysis was completed in this way without appreciable decomposition. The hydrochloric acid was removed as silver chloride in the usual way and the product was a pale yellow syrup (22·7 g.; $n_D^{20^\circ}$ 1·4595). This syrup was submitted to systematic fractional distillation through a specially designed, vacuum-jacketed column. The following fractions were ultimately separated :

Fraction.	Bath temp. and pressure.	Wt., g.	$n_D^{21^\circ}$.	OMe, %.
1	120—125°/0·07 mm.	4·9	1·4475	59·8
2	135—145 /0·07 mm.	2·8	1·4500	58·0
3	145—155 /0·10 mm.	4·3	1·4574	52·4
4	155—165 /0·10 mm.	2·7	1·4620	50·1
5	165—180 /0·05 mm.	1·2	1·4670	44·1
6	138—145 /0·04 mm.*	4·4	1·4705	41·1
7	Residue	1·4		

* Distilled without fractionating column : hence lower bath temperature.

Fractions 1, 3, and 6 consisted of tetramethyl methylmannopyranoside, trimethyl methylmannoside, and dimethyl methylmannoside respectively. By calculation from the refractive indices and methoxyl contents of fractions 2, 4, and 5 the compositions of these fractions were estimated, giving the following results : Fraction 2, 2·1 g. of tetramethyl methylmannoside and 0·7 g. of trimethyl methylmannoside; fraction 4, 1·9 g. of trimethyl methylmannoside and 0·8 g. of dimethyl methylmannoside; fraction 5, 0·3 g. of trimethyl methylmannoside and 0·9 g. of dimethyl methylmannoside. The still residue probably retained some dimethyl methylmannoside which could not be separated from the high-boiling residue owing to the decomposition of the latter when heated strongly enough to distil away the last traces of dimethyl methylmannoside (dimethyl methylmannoside was being collected in fraction 6 when the distillation had to be stopped owing to onset of decomposition in the flask). The composition of the mixture of hydrolysis products was therefore : Tetramethyl methylmannoside 7·0 g., trimethyl methylmannoside, 7·2 g., and dimethyl methylmannoside 6·1 g. In view of the difficulty experienced in collecting the last-named substance these results may be held to show that the hydrolysis product contained the three sugars in equimolecular proportions.

Proof of Identity of Tetramethyl Methylmannopyranoside.—Fraction 1 (4·8 g.) was heated with 2*N*-sulphuric acid (200 c.c.) at 95° for 4 hours. After neutralisation with barium carbonate the solution was evaporated under diminished pressure. The residue was extracted with boiling chloroform and after removal of the solvent tetramethyl mannose was obtained as a syrup (yield, 95% of the theoretical), $[\alpha]_D^{20^\circ}$ + 4° in water (*c*, 4·2), $n_D^{19^\circ}$ 1·4610.

When boiled with aniline, this syrup gave tetramethyl mannose anilide, which was recrystallised from ether (yield, 82% of the theoretical), m. p. alone or when mixed with an authentic specimen, 142—143° (Found: C, 61·3; H, 8·2; N, 4·8; OMe, 38·8. Calc. for $C_{16}H_{25}O_5N$: C, 61·7; H, 8·0; N, 4·5; OMe, 39·9%).

Another sample of the syrupy tetramethyl mannose was oxidised by bromine water at 40° for 80 hours. After aeration to remove bromine, neutralisation with silver carbonate to remove hydrobromic acid, and treatment with hydrogen sulphide to precipitate silver, the solution was evaporated, and the product extracted with chloroform. After removal of the chloroform a syrup was obtained (yield, 85% of the theoretical), which was distilled and the distillate was allowed to react with phenylhydrazine at 15° for 12 hours. This gave the phenylhydrazide of 2 : 3 : 4 : 6-tetramethyl mannonolactone, m. p. (after recrystallisation from benzene) 184—185°. Yield, 70% of the theoretical, calculated on the weight of tetramethyl mannose oxidised (Found: C, 56·0; H, 7·6; N, 8·4; OMe, 35·0. Calc. for $C_{16}H_{26}O_6N_2$: C, 56·1; H, 7·6; N, 8·2; OMe, 36·3%).

The phenylhydrazide was hydrolysed by heating it with $N/3$-sulphuric acid at 80° for 3 hours. After neutralisation (barium carbonate) the solution was extracted repeatedly with ether, the organic acid liberated by addition of the exact quantity of sulphuric acid, the solution evaporated to dryness (diminished pressure), and the product dissolved in chloroform. After removal of the chloroform a syrup remained which distilled at 100°/0·05 mm. The distillate (2 : 3 : 4 : 6-tetramethyl mannonolactone) crystallised immediately, m. p. 25°, $[\alpha]_D^{20°}$ + 150° in water (c, 2·0) (initial value; + 67°, final equilibrium value, attained after 100 hours at 15°) (Found: C, 51·2; H, 7·8; OMe, 50·5. Calc. for $C_{10}H_{18}O_6$: C, 51·3; H, 7·7; OMe, 53·0%).

Proof of Identity of 2 : 3 : 4-*Trimethyl Methylmannoside.*—(a) 2 : 3 : 4-*Trimethyl mannose.* A portion of fraction 3 (1·13 g.) was heated with $2N$-sulphuric acid at 95°, the reaction being followed polarimetrically: $[\alpha]_{5461}^{19°}$ + 54° (initial value); 45° (15 mins.); 38° (30 mins.); 33° (45 mins.); 29° (60 mins.); 24° (90 mins.); 19° (120 mins.); 16° (150 mins.); 14° (180 mins.); 12° (240 mins., constant value). This rate of hydrolysis is characteristic of a mannopyranoside. The solution was neutralised (barium carbonate) and evaporated to dryness (diminished pressure). The product was extracted with chloroform and on removal of the solvent 2 : 3 : 4-trimethyl mannose was obtained as a syrup (0·93 g.) which slowly crystallised; m. p. 102—103° (after recrystallisation from ether–light petroleum), $[\alpha]_D^{20°}$ + 7°, equilibrium value in water (c, 5·0) (Found: C, 49·0; H, 7·9; OMe, 41·8. Calc. for $C_9H_{18}O_6$: C, 48·7; H, 8·1; OMe, 41·9%).

(b) 2 : 3 : 4-*Trimethyl mannonolactone.* 2 : 3 : 4-Trimethyl mannose obtained by hydrolysis of fraction 3 was oxidised by bromine water in the usual way. The product was distilled, giving 2 : 3 : 4-trimethyl mannonolactone as a viscid non-reducing liquid, b. p. 135°/0·02 mm., $n_D^{12°}$ 1·4776, $[\alpha]_D^{20°}$ + 137° in water (c, 0·9) (yield, 50% of the theoretical). When kept, this syrup crystallised slowly but almost completely. The lactone was then recrystallised from ether, m. p. 91—92°, $[\alpha]_D^{20°}$ + 138° in water (c, 1·0) (initial value); 116° (10 hours); 99° (20 hours); 72° (40 hours); 55° (60 hours); 47° (80 hours); 45° (90 hours); 44° (110 hours, constant value). The rate of hydrolysis is characteristic of a δ-mannonolactone. The rotation of the corresponding acid, 2 : 3 : 4-trimethyl mannonic acid, $[\alpha]_D$ + 18° (c, 0·2), was determined by preparing a solution of the lactone in sodium hydroxide, acidifying it, and taking the rotation immediately. The lactone (0·10 g.) required 4·50 c.c. of $N/10$-sodium hydroxide for neutralisation (calc., 4·54 c.c.). The physical constants given here should replace those recorded by Haworth, Raistrick, and Stacey in the course of work on the syrupy lactone encountered during investigations on mannocarolose (Found: C, 49·0; H, 7·3; OMe, 42·0. $C_9H_{16}O_6$ requires C, 49·1; H, 7·3; OMe, 42·3%).

(c) 2 : 3 : 4-*Trimethyl mannosaccharic acid.* Further confirmation of the identity of the 2 : 3 : 4-trimethyl mannose was obtained by oxidising it with nitric acid (d 1·42) at 100° for 2 hours. The nitric acid was removed, and the product isolated as the methyl ester (for details of the method, consult previous papers from this laboratory), b. p. 110°/0·05 mm., $n_D^{14°}$ 1·4540 (yield, nearly quantitative). On treatment with methyl-alcoholic ammonia this ester gave 2 : 3 : 4-*trimethyl mannosaccharodiamide*, m. p. 191° (yield, almost quantitative) (Found: C, 43·2; H, 6·9; N, 11·3; OMe, 37·2. $C_9H_{18}O_6N_2$ requires C, 43·2; H, 7·2; N, 11·2; OMe, 37·2%).

Proof of Identity of 3 : 4-*Dimethyl Methylmannoside.*—A portion of fraction 6 was hydrolysed by heating it with $2N$-sulphuric acid at 95°, the reaction being followed polarimetrically: $[\alpha]_D^{18°}$ + 33° (initial value); 25° (15 mins.); 19° (30 mins.); 14° (45 mins.); 10° (60 mins.); 5° (90 mins.); 2·5° (120 mins.); 1° (180 mins.); ± 0° (240 mins., constant value). The rate of hydrolysis indicates the presence of a mannopyranoside structure. The acid was neutralised

with barium carbonate, the solution evaporated under diminished pressure, and the sugar dissolved in chloroform. Evaporation of the solvent left a syrup, which crystallised completely when left in contact with wet ether (yield, 80%). Recrystallisation from ether–ethyl acetate gave the *monohydrate* of 3 : 4-*dimethyl mannose*, m. p. 107—109°, $[\alpha]_D$ + 3°, equilibrium value in water (*c*, 1·8) (Found : C, 42·6; H, 7·45; OMe, 26·8. $C_8H_{16}O_6,H_2O$ requires C, 42·5; H, 7·2; OMe, 27·2%).

3 : 4-Dimethyl mannose monohydrate (1·2 g.) was oxidised by bromine water at 40° for 16 hours. The solution was then neutralised with silver carbonate and filtered (charcoal). The filtrate was rendered slightly acid with hydrochloric acid and, after filtration, was concentrated to a syrup under diminished pressure. The lactone was extracted by boiling chloroform and on removal of the solvent crystallised completely (yield, 80% of the theoretical). M. p. 157—158° (after recrystallisation from alcohol), $[\alpha]_D^{20°}$ + 174° in water, *c*, 1·0 (initial value); 160° (5 hours); 150° (10 hours); 145° (15 hours); 142° (20 hours); 135° (30 hours); 132° (40 hours); 129° (50 hours, constant value). The rate of hydrolysis indicates a δ-lactone. The rotation of 3 : 4-dimethyl mannonic acid in water was $[\alpha]_D^{20°}$ + 32° (*c*, 0·2). The *lactone* (0·1 g.) required 4·78 c.c. of *N*/10-sodium hydroxide for neutralisation (calc., 4·80 c.c.) (Found : C, 46·6; H, 7·2; OMe, 30·2. $C_8H_{14}O_6$ requires C, 46·6; H, 6·8; OMe, 30·1%).

When the lactone was allowed to react with methyl-alcoholic ammonia at 0° for 3 days, it was transformed almost quantitatively into 3 : 4-*dimethyl mannonamide*, m. p. 140° (after recrystallisation from a mixture of acetone, methyl alcohol and light petroleum). $[\alpha]_D^{20°}$ + 22° in water (*c*, 2·7). (The amide, therefore, does not follow the amide rotation rule; compare Harris, Hirst, and Wood, J., 1935, 1658.) When treated with sodium hypochlorite under standard and carefully controlled conditions (Weerman, *Rec. trav. chim.*, 1917, **37**, 16), the amide gave a copious yield of sodium cyanate, recognised in the usual way as hydrazodicarbonamide, m. p. 254° (yield, 40% of the theoretical). The amide therefore possessed a free hydroxyl group at C_2 [Found (for amide) : C, 43·3; H, 8·0; N, 6·1; OMe, 28·1. $C_8H_{17}O_6N$ requires C, 43·1; H, 7·6; N, 6·3; OMe, 27·7%].

Further evidence of the presence of a free hydroxyl group at C_2 was obtained from the preparation of an osazone without loss of methoxyl. Dimethyl mannose (0·2 g.), phenylhydrazine (0·4 c.c.), and glacial acetic acid (0·4 c.c.) were heated in water (10 c.c.) at 80° for 4 hours. A red oil separated which crystallised when kept at room temperature. Recrystallisation could not be carried out, the *osazone* separating always as an oil which subsequently crystallised. On this account the osazone could not be obtained analytically pure, but the figures given show clearly that the substance was an osazone containing two methoxyl groups (Found : C, 61·6; H, 6·6; OMe, 15·6. $C_{20}H_{26}O_4N_4$ requires C, 62·2; H, 6·7; OMe, 16·1%).

The presence of a methoxyl group at C_4 was indicated in the following way. Methylated derivatives of mannose in which the hydroxyl at C_4 is unsubstituted react readily with methyl-alcoholic hydrogen chloride in the cold, giving methyl mannofuranosides, the rotation first of all diminishing to a minimum negative value owing to the more rapid formation of the β-derivative at the beginning of the reaction. Thereafter the rotation slowly increases in the positive direction. When this reaction was tried with 3 : 4-dimethyl mannose monohydrate (0·4 g.) in 0·6% methyl-alcoholic hydrogen chloride (10 c.c.), the initial rotation ($[\alpha]_D^{20°}$ + 27°) remained unaltered during 60 hours and no formation of methylmannoside took place. The temperature was raised to 70° and the usual slow formation of a methylmannopyranoside was then observed : $[\alpha]_D^{20°}$ + 27° (initial value); 44° (4 hours); 57° (6 hours); 61° (8 hours); 64° (10 hours); 65° (12 hours); 67° (16 hours, constant value; solution non-reducing).

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161. *Polysaccharides. Part XXV. α-Amylodextrin.*

By W. N. HAWORTH, E. L. HIRST, H. KITCHEN, and S. PEAT.

IN an extended study, now proceeding, of the products of the action of amylolytic enzymes on starch occasion has arisen to examine more closely the limit dextrin produced by the action of β-amylase, the description applied by R. Kuhn to the enzyme of ungerminated grain. This dextrin, called variously α-amylodextrin and erythrogranulose, is formed, together with maltose, when the action of β-amylase on starch is allowed to proceed to

completion. The experiments recorded here support the observations of Hanes (*Canadian J. Res.*, 1935, **13**, 185), who found that α-amylodextrin is formed in 40% yield (calculated on the weight of starch), that the dextrin is homogeneous, is not degraded by β-amylase, and that the only other product of the amylolysis is maltose. Haworth, Hirst, and Waine (J., 1935, 1299), in an examination of α-amylodextrin, also record the striking fact that there is a complete cessation of the action of β-amylase on starch when the limit represented by 60% hydrolysis (calculated in terms of maltose produced) is reached. A gravimetric assay of methylated α-amylodextrin by the latter authors indicated a chain length of 16—17 glucose units for the dextrin. It was recognised that a discrepancy existed here in that a dextrin of this chain length could not be produced in 40% yield from a starch with a chain length of 24—30 glucose units if every chain had been uniformly degraded and it seemed possible that the discrepancy lay in the estimated chain length of the α-amylodextrin. A value of 11—12 units for the dextrin would more nearly represent the weight relationship between starch and the dextrin.

In view of the fact that a better yield of β-amylase is obtainable from wheat than from barley (von Klinkenberg, *Z. physiol. Chem.*, 1932, **209**, 253) the former source of β-amylase was used in this investigation. The enzyme was extracted by means of aqueous alcohol and was used in the form of an unbuffered aqueous solution. Although this solution (containing a crystal of thymol as preservative) lost very little of its amylolytic power on keeping over a period, a fresh preparation was usually made for each series of experiments. A commercial soluble starch was employed as substrate, investigation having shown that the cold aqueous acid treatment used in its preparation does not appreciably degrade the 24—30 unit glucose chain. Further slight variations in the experimental procedure of Haworth, Hirst, and Waine were introduced. The starch enzyme mixture was incubated at 38° instead of at 55°, no buffer was employed, and the adjustment of acidity to p_H 6 was not made. The small amount of mineral acid contained in the soluble starch was sufficient to maintain the hydrolysis mixture slightly on the acid side of neutrality. The course of the hydrolysis was followed by estimation of the increase in reducing power of the solution (by a copper reduction method). At completion, the copper number corresponded to the liberation of 62—63% of maltose. From the hydrolysis mixture were isolated α-amylodextrin and crystalline maltose and no other product, the yields by weight being respectively 40% and 50%.

The α-amylodextrin so prepared is identical with that prepared by Haworth, Hirst, and Waine in respect of solubility, colour with iodine, iodine number, phosphorus content and in resistance to the further action of β-amylase. Nevertheless a difference is observed in the optical activity of the two dextrins: the dextrin now described has $[\alpha]_D^{20^\circ}$ + 167·0° in water (+ 133·0° in aqueous sodium hydroxide), whereas that prepared by Haworth, Hirst, and Waine shows $[\alpha]_D^{20^\circ}$ + 200° in water (+ 144° in aqueous sodium hydroxide). Moreover, this difference persists in the methylated dextrins. Haworth, Hirst, and Waine record for methylated α-amylodextrin, $[\alpha]_{5780}^{19^\circ}$ + 222°, whereas here the value found is $[\alpha]_D^{25^\circ}$ + 197·2° (maximum). Further investigation may reveal the cause of this difference.

The gravimetric assay of the end group has been made on three specimens of methylated α-amylodextrin, each prepared by a different method. The first was obtained by the simultaneous deacetylation and methylation of a triacetate which had been prepared by the action of pyridine and acetic anhydride on α-amylodextrin. Acetylation of the dextrin in the presence of chlorine and sulphur dioxide yielded an acetate which differed from the first only in that it gave more viscous solutions in chloroform. Deacetylation and methylation of this acetate proceeded smoothly and gave methylated α-amylodextrin. The third specimen was prepared by the direct treatment of α-amylodextrin with the methylating agents, the intermediate formation of an acetate being omitted. The methylations were all carried out at room temperature and the three specimens of methylated α-amylodextrin were closely similar in properties. Each was separately hydrolysed by boiling with methyl-alcoholic hydrogen chloride and the proportions of tetramethyl methylglucoside so formed were estimated as 9·8, 10·5, and 10·4% respectively of the weight of methyl derivative. The chain length of the methylated dextrin is thus, in each case, 11—12 glucose units. Obviously the α-amylodextrin suffers no degradation under the action of the acetylating agents, since direct methylation in alkaline solution, where no hydrolysis of glucosidic

links can occur, yields a methylated dextrin of the same chain length as those prepared from the acetates. It is reasonable to conclude, therefore, that the α-amylodextrin from which these derivatives are prepared is also composed of a chain of 11—12 glucopyranose units. We are of the opinion that the specimen forming the subject of the present work was the genuine α-amylodextrin and that the material described by Haworth, Hirst, and Waine (*loc. cit.*) may not have been identical with it. The viscosity data indicate that the molecules of α-amylodextrin are aggregated in the manner observed with starch and other polysaccharides (compare Haworth, Hirst, and Isherwood, this vol., p. 577) and discussion of the mode and degree of aggregation will be the subject of future communications.

EXPERIMENTAL.

Preparation of β-Amylase.—The procedure of Hanes (*Biochem. J.*, 1936, **30**, 168) was adopted for the extraction of β-amylase from ungerminated wheat. The wheat, ground to a fine flour, was twice extracted by stirring with 50% aqueous alcohol, and the enzyme precipitated from the clear extract by increasing the alcohol concentration to 80%. The precipitate, separated on the centrifuge and freed from alcohol by suction, was dissolved in water (450 c.c. for the extract from 200 g. of flour) and filtered. The clear solution, to which a crystal of thymol was added as a preservative, was utilised as the source of β-amylase in the following experiments. The solution gave a negative Wijsman test (*Rec. trav. chim.*, 1890, **9**, 1) for α-amylase.

Preparation of α-Amylodextrin.—The starch was a commercial soluble starch which had undergone no degradation in the process of solubilisation. The starch gave a blue colour with iodine. The iodine number was 1·3; phosphorus (as P_2O_5), 0·22%; $[\alpha]_D^{21°}$ + 148·0° in 5% aqueous sodium hydroxide (*c*, 1·5, dried sample); moisture content, 12% and ash, 0·35%. The soluble starch contained a small amount of mineral acid equivalent to 20·0 c.c. of 0·1*N*-sodium hydroxide per 100 g.

The following is a typical example of the method used: Soluble starch (50 g.) was stirred into cold water (100 c.c.) and the thin cream so produced was poured into boiling water (400 c.c.). The resulting gel was cooled and mixed with the standard solution of β-amylase (200 c.c.), and the mixture incubated at 38°. The starch paste rapidly liquefied and after 30 minutes a very small amount of a flocculent precipitate separated. This precipitate appeared to be of protein nature and was discarded. The course of the hydrolysis was followed by a copper-reducing method (*J. Soc. Chem. Ind.*, 1925, **44**, 150T). After 24 hours no further increase occurred in the reducing powder of the solution, which corresponded to a conversion of 62—63% of the starch into maltose. Alcohol (2 l.) was added to the solution and the grey sticky precipitate was hardened by refluxing with absolute alcohol. The crude dextrin so obtained was purified by solution in water (400 c.c.), precipitation by addition of alcohol (2 l.), filtration, and washing with alcohol and ether. Finally it was dried in a vacuum. The α-amylodextrin was a white non-reducing powder which was soluble in cold water. The solution was turbid but became clear on boiling. No gel formation was observed. The α-amylodextrin gave a purple coloration with iodine and showed iodine number 2·7; P_2O_5, 0·40%; $[\alpha]_D^{20°}$ + 167·0° in water (*c*, 2·0) and $[\alpha]_D^{24°}$ + 133·0° in 5% aqueous sodium hydroxide (*c*, 1·4). Numerous experiments demonstrated that β-amylase was without action on this dextrin.

The combined filtrates from the precipitation and purification of the α-amylodextrin were concentrated under diminished pressure to a thick syrup, which was repeatedly extracted with boiling methyl alcohol. A small insoluble residue was added to the dextrin fraction. The methyl-alcoholic extract was concentrated to a syrup, which crystallised on standing for 12 hours in contact with one-tenth of its volume of water. The crystalline product showed $[\alpha]_D^{20°}$ + 11·7° ⟶ + 127·4° in water (*c*, 0·6); m. p. 110° (decomp.), and iodine number 55·3 (calc. for maltose hydrate, 55·5) (Found: C, 40·5; H, 7·0. Calc. for maltose hydrate: C, 40·0; H, 6·7%). It formed an osazone, m. p. 200° (decomp.); $[\alpha]_D^{20°}$ + 58·0° in methyl alcohol (*c*, 1·4), which was microscopically identical with maltosazone (Found: N, 10·3. Calc. for $C_{24}H_{32}O_9N_4$: N, 10·8%). The yields, by weight, of α-amylodextrin and crystalline maltose were respectively 40% and 50% of the original starch (corrected for moisture content).

Acetylation of α-Amylodextrin.—(a) *By pyridine and acetic anhydride.* The air-dried dextrin (50 g.) was shaken for 12 hours with pyridine (200 g.) and a cold mixture of pyridine (200 g.) and acetic anhydride (300 g.) was then added with stirring. In 3 hours at room temperature complete solution of the dextrin was attained and the acetate was precipitated by stirring the solution slowly into cold water (10 vols.). The white granular precipitate was collected on cloth, washed with hot water until acid-free, and dried in the usual way. The acetate was readily and

completely soluble in acetone, chloroform, *m*-cresol and anisole, was non-reducing, and showed $[\alpha]_D^{20°}$ + 155·0° in chloroform (*c*, 0·9); iodine number, 1·4; P_2O_5, 0·20% (Found: CH_3·CO, 39·0. Calc. for $C_{12}H_{16}O_8$: CH_3·CO, 44·8%). The specific viscosity was 0·190 (*c*, 0·8) in *m*-cresol, corresponding to an apparent molecular weight of 6840 ($K_m = 1 \times 10^{-3}$) or 24 glucose units.

(b) *By acetic anhydride in the presence of sulphur dioxide and chlorine.* α-Amylodextrin (70 g.), 'activated' by precipitation from an aqueous solution by alcohol, was suspended in glacial acetic acid (450 g.) containing a little chlorine. After ½ hour, acetic anhydride (750 g.) containing an amount of sulphur dioxide equivalent to the chlorine was added with stirring. The mixture was maintained at 60° for 5 hours and was then poured into cold water (10 vols.). The precipitated acetate was separated, washed, and dried in the usual way. Yield, 20 g. The acetate was non-reducing and gave no coloration with iodine solution; $[\alpha]_D^{20°}$ + 162·0° in chloroform (*c*, 5·0); iodine number, 1·8; $\eta_{sp.}^{20°}$ 0·180 (*c*, 0·4), corresponding to an apparent molecular weight of 13,000 or 45 glucose units (Found: CH_3·CO, 44·0. Calc. for $C_{12}H_{16}O_8$: CH_3·CO, 44·8%).

Methylated α-Amylodextrin.—(a) *Methylation of the acetate prepared by the pyridine method.* The α-amylodextrin acetate (50 g.) was dissolved in acetone (700 c.c.) and treated in the cold with methyl sulphate (300 c.c.) and 30% aqueous sodium hydroxide (800 c.c.) over a period of 5 hours. The mixture was then neutralised and boiled, the partly methylated dextrin being precipitated. This methylation process was repeated nine times, and the product finally treated once with methyl iodide and silver oxide. The following properties were recorded:

No. of methylations:	1.	2.	4.	6.	8.	9.	10.
$[\alpha]_D^{25°}$ in $CHCl_3$	+160°	+159·2°	+195·0°	+180·0°	+197·2°	+184·5°	+190·8°
OMe, %	24·2	32·8	39·6	42·5	43·7	44·0	44·1
$\eta_{sp.}^{20°}$ in *m*-cresol (*c*, 0·4)	—	0·130	0·126	0·096	0·086	0·097	0·113
M, from viscosity ($K_m = 10^{-3}$)	—	6500	6300	4900	4400	4800	5700

The final product was purified by fractionation in a chloroform–light petroleum mixture. A small first fraction was discarded; the main fraction was dried in a vacuum and used in the experiments to be described, where it is referred to as methyl dextrin A.

(b) *Methylation of the acetate prepared by using chlorine and sulphur dioxide as catalysts.* The acetate (20 g.) was dissolved in acetone (600 c.c.) and treated with the methylating reagents (see above) at room temperature. After eight methylations the product—methyl dextrin B—showed (after purification by precipitation, chloroform–light petroleum) OMe, 44·8%; $[\alpha]_D^{17°}$ + 194·9° in chloroform (*c*, 1·3); $\eta_{sp.}^{20°}$ 0·153 in *m*-cresol (*c*, 0·4), corresponding to *M*, 7800. Yield, 20 g.

(c) *Methylation of α-amylodextrin directly.* α-Amylodextrin (35 g.) was dissolved in dilute aqueous sodium hydroxide and treated in the cold with methyl sulphate (300 c.c.) and 30% aqueous sodium hydroxide (800 c.c.) in the manner described above. After eight methylations, the product had OMe, 45·0%; $[\alpha]_D^{18°}$ + 194·3° in chloroform (*c*, 2·0) and $\eta_{sp.}^{20°}$ 0·195, corresponding to an apparent molecular weight of 10,000. Yield, 35 g. The product was fractionated by solution in chloroform and precipitation with light petroleum. The main fraction—methyl dextrin C—showed OMe, 44·4%; $[\alpha]_D^{18°}$ + 194·0° in chloroform (*c*, 1·5) and $\eta_{sp.}^{20°}$ 0·200 in *m*-cresol (*c*, 0·4), corresponding to *M*, 10,200.

Determination of the Chain Length of α-Amylodextrin by the End-group Method.—(a) *Hydrolysis of methyl dextrin A.* The dry methylated α-amylodextrin (10·0 g.) was heated, under reflux, with methyl alcohol (150 c.c.) containing dry hydrogen chloride (2% by weight) until the optical rotation became constant (4½ hours). The clear solution was neutralised with dry silver carbonate, filtered, and the solvent removed, under diminished pressure, from the filtrate. The residual syrup was purified by solution in ether, filtration, and removal of the solvent. Yield, 10·3 g. of mixed glucosides (90% of the theoretical). The syrup was now fractionated by slow distillation at 0·05 mm. pressure from a Widmer flask bearing a short vacuum-jacketed fractionating column. The properties of the fractions were as follows:

Fraction:	1.	2.	3.	4.	5.	6.
Weight, g.	0·81	0·40	0·78	1·41	2·96	1·92
$n_D^{20°}$	1·4453	1·4510	1·4559	1·4580	1·4584	1·4612
OMe, %	60·0	56·2	53·0	52·0	51·1	49·2

The methoxyl content justifies the assumption that fraction 4 consists entirely of trimethyl methylglucoside (Calc.: OMe, 52·6%) and that fraction 1 is not entirely tetramethyl methyl-

glucoside (OMe, 62·0%). The refractive indices of the fractions indicate that the content of tetramethyl methylglucoside ($n_D^{20°}$ 1·4430) in fractions 1, 2, and 3 are respectively 84·7, 46·6, and 1·4%. The total weight of tetramethyl methylglucoside (including a 10% correction for losses; see Haworth and Machemer, J., 1932, 2270) is 0·977 g., consistent with a chain length of 12 glucose units for methyl dextrin A.

(b) *Hydrolysis of methyl dextrin B.* The procedure adopted in the hydrolysis of methyl dextrin B (13·7 g.) was the same as that described under (a). The greater part (11·3 g.) of the mixed glucosides (14·0 g.) was distilled into a Widmer flask and this part (containing the whole of the tetramethyl methylglucoside) was carefully fractionated by slow distillation at 0·10 mm. pressure, as follows :

Fraction :	1.	2.	3.	4.	5.
Weight, g.	0·68	0·33	0·56	1·01	8·69
$n_D^{19°}$	1·4430	1·4462	1·4511	1·4553	1·4572
OMe, %	61·8	59·3	55·8	53·0	52·4

The methoxyl contents indicate that fractions 1 and 5 consist respectively of pure tetramethyl methylglucoside and pure trimethyl methylglucoside and from the refractive indices it was estimated that fractions 2, 3, and 4 contained respectively 77·5, 43·0, and 13·4% of tetramethyl methylglucoside. The total yield of the latter glucoside (with the 10% correction) was 1·440 g., *i.e.*, 10·5% by weight of the original methyl dextrin, the chain length of which is thus shown to be 11—12 glucose units.

(c) *Hydrolysis of methyl dextrin C.* The dried dextrin (20·0 g.), submitted to the action of methyl-alcoholic hydrogen chloride under the conditions described above, yielded 20·2 g. of the mixed glucosides, which, on distillation from a Widmer flask at 0·01 mm. pressure, were separated into the following fractions :

Fraction :	1.	2.	3.	4.	5.
Weight, g.	1·30	0·40	0·46	1·6	7·8
$n_D^{20°}$	1·4428	1·4462	1·4494	1·4554	1·4560
OMe, %	61·6	59·7	57·3	53·0	52·3

Fraction 1 consists solely of tetramethyl methylglucoside, fraction 5 of pure trimethyl methylglucoside, and fractions 2, 3, and 4 contain respectively 74·3, 50·0, and 4·6% of tetramethyl methylglucoside, the yield of which (with the 10% correction) is 10·45% of the weight of methyl dextrin. This value corresponds to a chain length of 11—12 units. In all three experiments the identity of the products was established by acid hydrolysis of the appropriate fractions and isolation of crystalline 2 : 3 : 6-trimethyl glucopyranose and crystalline 2 : 3 : 4 : 6-tetramethyl glucopyranose.

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162. *Acetone Derivatives of Gluconic Acid.*

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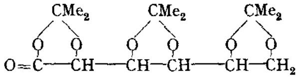
IT should be possible theoretically to protect all the hydroxyl groups, including the carboxyl, in gluconic acid by condensation with acetone. Despite the *cis*- or *trans*-disposition of these groups with respect to one another in the conventional projection formula of gluconic acid it is clear that, allowing free rotation round the single-bonded carbon atoms, the addenda would take up appropriately *cis*-positions such as may be required for condensation with acetone. An atom model makes this point clear. This expectation is realised in the formation of both *gluconic acid diacetone* and *gluconic acid triacetone*, which are isolated as crystalline substances. The latter can also be converted into the former by mild hydrolytic agents. There can be little doubt that in the diacetone the positions 1 and 2 are unsubstituted, since 2-methyl gluconic acid was obtained by its methylation and subsequent hydrolysis. By the use of atom models it is shown that fifteen triacetone gluconic acids are theoretically possible, but, for the reasons stated on p. 797, only two of the models, namely, those showing the acetone groups at 1 : 2, 3 : 4, 5 : 6, or at 1 : 2, 3 : 5,

4 : 6, seem very probable structurally. On general grounds it would appear that the most likely formulation is that annexed.



Experimental.

Gluconic Acid Di- and Tri-acetone.—Finely powdered calcium gluconate (40 g.), anhydrous copper sulphate (35 g.), and acetone (800 c.c.) were intimately mixed and the calculated quantity of sulphuric acid (*d* 1·84) required to transform the calcium salt into gluconic acid was added. The mixture was shaken for 100 hours and was then filtered. The filtrate on concentration under diminished pressure gave a thin syrup, which partly crystallised. The solid was recrystallised from boiling light petroleum (1 l.), giving long white needles (2·4 g.) of *gluconic acid diacetone*, m. p. 154°, $[\alpha]_D^{18°}$ + 11° in ethyl alcohol (*c*, 1·84). This substance was soluble in water, alcohol and ether, the aqueous solution being distinctly acid in its reactions (Found : C, 52·2; H, 7·2; Me_2CO, 42·7. $C_{12}H_{20}O_7$ requires C, 52·2; H, 7·3; Me_2CO, 42·0%).

The petroleum mother-liquors were evaporated to a thin syrup, which partly crystallised. The solid on recrystallisation from light petroleum gave large colourless rhombic crystals of *gluconic acid triacetone* (1·6 g.), insoluble in water, easily soluble in alcohol and ether; m. p. 111°, $[\alpha]_D^{18°}$ + 31° in ethyl alcohol (*c*, 1·98) (Found : C, 57·1; H, 7·7; Me_2CO, 53·9. $C_{15}H_{24}O_7$ requires C, 57·0; H, 7·6; Me_2CO, 55·1%). An aqueous alcoholic solution was neutral to litmus.

Gluconic acid triacetone may be prepared more conveniently by the following method. Calcium gluconate (20 g.) was shaken with acetone (400 c.c.) containing concentrated sulphuric acid (3 c.c.) for 100 hours at room temperature. The filtered solution was neutralised with silver carbonate and concentrated under diminished pressure to a thin syrup, which partly crystallised. Recrystallisation of the solid from light petroleum gave gluconic acid triacetone (3·0 g.), m. p. 111°. The petroleum mother-liquors contained a small quantity (0·4 g.) of the diacetone derivative.

Gluconic acid diacetone may be obtained in very poor yield from the triacetone compound by careful hydrolysis in methyl alcohol containing 0·05% of hydrochloric acid. After 8 hours at 45°, when the rotation was $[\alpha]_D$ + 13° (initial value + 30°), the solution was neutralised (silver carbonate) and evaporated to a syrup, which slowly deposited crystals of gluconic acid diacetone, m. p. 154°.

2-Methyl Gluconic Acid Diacetone.—Gluconic acid diacetone (4·6 g.), dissolved in methyl iodide (40 c.c.) containing methyl alcohol (1 c.c.), was boiled for 3 hours with silver oxide (28 g.). The product was extracted by boiling ether and on removal of the solvent was obtained as a mobile syrup (5 g.), which was twice methylated by silver oxide and methyl iodide and then distilled, giving a mobile oil (4·7 g.), b.p. 105°/0·02 mm. This rapidly crystallised, giving *methyl 2-methylgluconate diacetone* in large plates, which were recrystallised from light petroleum; m. p. 44°, $[\alpha]_D^{19°}$ + 41° in water (*c*, 1·25). The ester was soluble in water and in organic solvents, and 0·1247 g. required for hydrolysis 4·3 c.c. of *N*/10-sodium hydroxide (calc., 4·1 c.c.) (Found : C, 55·4; H, 8·0; OMe, 20·7. $C_{14}H_{24}O_7$ requires C, 55·3; H, 8·0; OMe, 20·4%).

Methyl 2-methylgluconate diacetone was hydrolysed by heating its solution in 2% hydrochloric acid at 50° for 2 hours; the product was isolated in the usual way. *2-Methyl γ-gluconolactone* was thus obtained as a colourless syrup which resisted crystallisation. The rotation data are therefore given with reserve : $[\alpha]_D$ + 45° (initial value), 37° (after 7 days; constant value) (Found : OMe, 14·8. $C_7H_{12}O_6$ requires OMe, 16·1%). The lactone (1·8 g.) was dissolved in methyl alcohol saturated at 0° with ammonia. No precipitate formed and the absence of gluconic acid was thereby established. After some hours at room temperature the solvent was evaporated, leaving a solid but extremely hygroscopic residue, which was recrystallised from dioxan (yield, 1·2 g.). *2-Methyl gluconamide* was then obtained as a white microcrystalline powder, m. p. 139°, $[\alpha]_D^{18°}$ + 39° in water (*c*, 0·34). The amide was exceedingly hygroscopic and was freely soluble in water and in alcohol (Found : N, 6·6; OMe, 14·3. $C_7H_{15}O_6N$ requires N, 6·7; OMe, 14·8%).

When the amide was treated with aqueous sodium hypochlorite under the conditions prescribed by Weerman (*Rec. trav. chim.*, **1917**, **37**, 16), several hours elapsed before there was a sensible diminution of the strength of the hypochlorite. The excess of hypochlorite was then removed and a solution of semicarbazide hydrochloride in concentrated aqueous sodium acetate

was added. No precipitate formed, even after several hours. In another experiment the solution, after reaction with the hypochlorite, was treated with hydrazine sulphate and neutralised, and benzaldehyde added. The resulting yellow precipitate (benzaldehydehydrazone) was completely soluble in ether and contained no benzaldehydesemicarbazone. The methoxy-group in the amide was therefore at position 2. Control experiments with gluconamide and the same solution of sodium hypochlorite gave copious yields of hydrazocarbonamide (m. p. 256°) and benzaldehydesemicarbazone (m. p. 220°) respectively.

X-*Ray Examination of Triacetone Gluconic Acid* (By E. G. Cox and C. J. Brown).

This substance forms large columnar crystals of orthorhombic symmetry, usually elongated parallel to the c axis. The forms $a\{100\}$, $m\{110\}$, and $o\{111\}$ were observed. By means of X-ray measurements the unit-cell dimensions were found to be $a = 14{\cdot}62$, $b = 13{\cdot}22$ and $c = 8{\cdot}83$ A., so that there are four molecules in the unit cell and d (calc.) $= 1{\cdot}23$ g./c.c. The birefringence is low, the mean refractive index for sodium light being 1·48.

Examination of models shows that at least eight of the fifteen theoretically possible triacetone gluconic acids can be obtained in strainless forms; of these, however, five involve seven-, eight-, or nine-membered rings. Of the remaining three, one (1 : 3, 2 : 4, 5 : 6) involves a somewhat improbably close juxtaposition of various atoms, so that it is very probable that triacetone gluconic acid has one of the remaining two structures, namely, 1 : 2, 3 : 4, 5 : 6 or 1 : 2, 3 : 5, 4 : 6. Unfortunately the X-ray data available do not enable a decision between these two to be made.

University of Birmingham, Edgbaston. [*Received, March 25th*, 1937.]

163. *The Estimation of* cyclo*Pentadiene and Indene, and their Polymerisation in Carbon Tetrachloride Solution.*

By D. Ll. Hammick and (Miss) D. Langrish.

Although pure *cyclo*pentadiene and indene polymerise rapidly under ordinary conditions, the rate of polymerisation might be expected to diminish on solution in an inert solvent. The work now described was carried out to see how far this prediction is in accordance with fact, and in the hope that conditions might be found under which the rate of polymerisation is so slow that the rate of interaction of these hydrocarbons with additive reagents such as nitro-compounds could be measured without ambiguity (Hammick and Sixsmith, J., 1935, 580). The first step in the investigation was the working out of a method of analysis which would give a sufficiently rapid and accurate estimate of unimolecular forms present in solutions containing mixtures of monomer and dimer. Such a method was found in a variant of the several analytical processes depending upon the quantitative addition of bromine to unsaturated substances. The use of an acidified solution of potassium bromide and bromate as the source of bromine (Francis, *Ind. Eng. Chem.*, 1926, **18**, 821) is unsatisfactory because acid is known to catalyse polymerisation (Stobbe and Färber, *Ber.*, 1924, **57**, 1838; Schultze, *J. Amer. Chem. Soc.*, 1934, **56**, 1552). We find, however, that dilute solutions (up to about $M/20$) of *cyclo*pentadiene and of indene in carbon tetrachloride absorb accurately and rapidly two atoms of bromine from excess bromine also in carbon tetrachloride. As is shown in the experimental part, the amount of the excess must be controlled (twice the calculated amount) in the case of indene.

With the above technique the estimation of unimolecular indene in presence of its dimer is simple, because, although the latter is unsaturated, its rate of reaction with bromine is very slow (Staudinger, *Helv. Chim. Acta*, 1929, **12**, 934). On the other hand, di*cyclo*pentadiene reacts as rapidly with one molecule of bromine as does *cyclo*pentadiene itself. It is easily shown, however, that if there are a g.-mols. of *cyclo*pentadiene initially present in a litre of solution and if b g.-mols. of dimer are formed, then the number of atoms of bromine that can be absorbed per litre is $2(a - b)$.*

* The concentration of the unimolecular form is $a - 2b$ g.-mols./l.; this reacts with $2(a - 2b)$ g.-atoms of bromine, and b g.-mols. of dimer react with $2b$ g.-atoms of bromine. Hence, the total number of g.-atoms of bromine required for reaction is $2(a - 2b) + 2b = 2(a - b)$.

It has long been known that indene absorbs oxygen (Thiele, *Ber.*, **1900**, **33**, 3393), and Davis, Crandall, and Higbee (*Ind. Eng. Chem.*, **1931**, **23**, 108) found that the presence of oxygen prevented accurate estimation by the aqueous bromide–bromate method. A similar effect was noticed by Schultze (*loc. cit.*) with *cyclo*pentadiene. We find that solutions of these two hydrocarbons in carbon tetrachloride contain no peroxides when freshly made up with the pure unimolecular forms, negative results being obtained by Kharasch's test (*J. Amer. Chem. Soc.*, 1933, **55**, 2468). On keeping in contact with air, these solutions polymerise slowly, and we have followed the process by titration with bromine. The polymerisation is accompanied by the development of a positive Kharasch test for peroxides. We find, moreover, that the rate of polymerisation is diminished by the progressive addition of the antoxidant acetonitrile to the solutions, becoming zero in acetonitrile itself. The inference to be drawn from these facts is that the polymerisation mechanism involves oxygen. Confirmation of this view comes from the fact that solutions of *cyclo*pentadiene and of indene, prepared and preserved in an atmosphere of nitrogen, do not polymerise. Polymerisation begins, however, after oxygen has entered the systems, its presence being revealed as peroxide.

EXPERIMENTAL.

I. *Experiments with* cyclo*Pentadiene.*—(1) *Preparation of solutions of pure* cyclo*pentadiene.* Pure *cyclo*pentadiene was obtained by the distillation of a commercial specimen, which contained a considerable proportion of di*cyclo*pentadiene. The crude hydrocarbon was placed in a round-bottomed flask fitted with a Dufton-type fractionating column (1 m. long). A stream of dry nitrogen (freed from traces of oxygen by passage, after admixture with 5% of hydrogen, over heated platinised asbestos) was passed for an hour through the apparatus. The hydrocarbon was then distilled slowly in the nitrogen stream, the fraction of b. p. 40—41°/755 mm. being collected. A fitting at the bottom of the condenser enabled the distillate to be collected in either of two receivers, so that the required fraction could be obtained without letting air into the apparatus. Small portions of the fresh distillate were immediately transferred to a tared standard flask (50 c.c.) containing about 25 c.c. of carefully purified and dried carbon tetrachloride. After being weighed, the solutions were made up to 50 c.c. with pure tetrachloride.

Estimation of cyclo*pentadiene in freshly prepared solution in carbon tetrachloride.* The bromine used in the estimations was purified (Cohen, *J. Amer. Chem. Soc.*, 1930, **52**, 2827) by shaking with *N*/10-sodium hydroxide, and distilled from phosphoric oxide in an all-glass apparatus. Solutions were made up in pure carbon tetrachloride (*ca.* *N*/10) and standardised by titration with standard thiosulphate after shaking with potassium iodide solution. 5, 10, or 20 C.c. portions of the *cyclo*pentadiene solutions, prepared as described above, were run (from standardised pipettes) into small conical flasks, and to them various excesses of bromine solution were added. After mixing, the solutions were at once shaken with aqueous potassium iodide, the liberated iodine being titrated with standard thiosulphate (*N*/10 or *N*/100). The figures in Table I show the kind of accuracy attained under the conditions indicated. The first and the last two of the tabulated experiments were carried out with 10 c.c. of solution; the remainder with 5·0 c.c.

TABLE I.

C_5H_6 (g.-mols./l.)	0·0395	0·2976	0·0872	0·02976	0·02976	0·01296	0·03420
Br added, as c.c. of *N*/10	11·05	5·505	4·84	5·505	5·505	6·600	18·60
Excess Br, in terms of *N*/10-$Na_2S_2O_3$, c.c.	7·60	2·57	3·95	2·59	2·62	1·42	4·96
C_5H_6 (*g.-mols./l.) found*	0·0385	0·02965	0·0872	0·02944	0·02916	0·01295	0·03410

Rate of polymerisation of cyclo*pentadiene in carbon tetrachloride at* 25°: *stabilising effect of acetonitrile.* In Table II are the results of a number of experiments on the rate of polymerisation of *cyclo*pentadiene in carbon tetrachloride, the amount of unimolecular form present at any time t (in hours) being found by reaction with bromine as described above. From the number of g.-atoms of bromine absorbed by aliquot portions of solution, the concentration (in g.-mols./l.) of unimolecular *cyclo*pentadiene present was found by the use of the relation already derived. The velocity constants k were calculated by means of the equation $k_* = (1/t)x/a(a - x)$, where a is the initial concentration of *cyclo*pentadiene and x is the amount of it polymerised after time t ($x = 2b$, where b is the number of g.-mols. of dimer: see above).

A solution of 0·00872 g.-mols. of *cyclo*pentadiene in pure acetonitrile underwent no alteration in bromine value after keeping for 8 days.

Peroxide formation in cyclo*pentadiene solutions.* The Kharasch test (*loc. cit.*) for peroxides in specimens of unsaturated compounds that have been exposed to air consists in shaking them with a colourless aqueous solution of ferrous ammonium sulphate and ammonium thiocyanate; production of the characteristic ferric thiocyanate coloration shows the presence of peroxide. All solutions of *cyclo*pentadiene in carbon tetrachloride that had been kept for any length of time gave a positive test for peroxide, and a freshly prepared solution (*ca.* 0·1*M*) gave a faint coloration after 15—20 minutes' contact with the air.

TABLE II.

a = 0·02976 g.-mols./l.

Time	16	28	44	53	68
C.c. of *N*/190-Br absorbed by 5·00 c.c.	28·3	27·3	26·6	25·8	25·2
Concn. of diene	0·0269	0·0248	0·0234	0·0218	0·0206
k	0·223	0·238	0·207	0·227	0·219

a = 0·02976 g.-mols./l.: solution contained 1% acetonitrile by vol.

Time	28	52	118	139	169
C.c. of *N*/100-Br absorbed by 4·95 c.c.	28·3	27·4	25·9	25·6	25·8 *
Concn. of diene	0·0274	0·0256	0·0226	0·0216	0·0202
k	0·096	0·105	0·091	0·092	0·091

* Absorbed by 5·13 c.c. of diene solution.

a = 0·02976 g.-mols./l.: solution contained 5% acetonitrile by vol.

Time	5	22	43	118	140
C.c. of *N*/100-Br absorbed by 4·95 c.c.	29·05	28·65	27·35	26·40	25·71
Concn. of diene	28·92	28·14	26·67	23·15	22·12
k	0·083	0·088	0·0895	0·081	0·082

a = 0·03385 g.-mols./l.: solution contained 20% acetonitrile by vol.

Time	50	72	120	147	168
C.c. of *N*/100-Br absorbed by 4·95 c.c.	32·15	31·50	30·40	29·90	28·55
Concn. of diene	31·12	29·80	27·58	26·60	26·10
k	0·052	0·056	0·056	0·055	0·052

We give below the results of an attempt to keep a solution in contact with pure nitrogen for some days. It is seen that after 48 hours oxygen had begun to get in, as shown by a positive peroxide test, although the bromine estimation of hydrocarbon shows no change from the original value. After 70 hours a strong Kharasch reaction was shown and polymerisation had set in.

Time (hours)	0	0·5	24	48	70
Concn. of diene	0·0522	0·0522	0·0523	0·0522	0·0494
Kharasch test	−	−	−	+	++

II. *Experiments with Indene.—Preparation of solutions of pure indene in carbon tetrachloride.* A commercial specimen of indene was distilled twice through a small fractionating column. In the first distillation the fraction of b. p. 178—180° was collected. This was redistilled, and portions of the fraction of b. p. 179—180° were collected in tared flasks. After being weighed, these portions were made up to known volumes with pure carbon tetrachloride.

Estimation of indene in carbon tetrachloride solution. The method used for the estimation of indene was in principle that already described for the estimation of *cyclo*pentadiene; but whereas in the latter case the addition of any convenient excess of bromine in carbon tetrachloride, followed immediately by the estimation of the unreacted bromine, gave satisfactory results, in the case of indene solutions a rather more rigid technique must be followed. It is necessary to have the concentration of the indene to be estimated in the neighbourhood of 0·05 g.-mol./l. (*i.e.*, *ca.* *N*/10), and to add about twice the stoicheiometric amount of bromine in carbon tetrachloride. If the concentration of indene is much above 0·05*M*, more than the theoretical amount of bromine is absorbed; under these conditions some substitution takes place, as is shown by the presence of hydrobromic acid in the solution.

The actual method of estimation consisted in running a known volume of a carbon tetrachloride solution of indene from a standardised pipette into a clean, dry flask and adding pure solvent until the solution was approximately *N*/10 (*M*/20). A measured volume of a standard solution of bromine in carbon tetrachloride was then run in, about 2 equivs. of bromine being added to 1 equiv. of indene. After not longer than half a minute, with shaking, aqueous

potassium iodide was added. The iodine liberated after vigorous shaking was estimated with standard ($N/10$) thiosulphate. In Table III are collected results of experiments illustrating the necessity for the technique prescribed above, and the accuracy attained when it is followed.

TABLE III.

Various freshly prepared solutions of indene in carbon tetrachloride were treated with (*a*) slight excess, (*b*) large excess of bromine solution.

C_9H_8 (g.-mols./l.).	Vol. of indene soln., c.c.	Br added, as c.c. of $N/10$.	Excess Br, as $N/10$-$Na_2S_2O_3$, c.c.	C_9H_8 (g.-mols./l.) found.
0·0437	(*a*) 10·0	12·43	4·65	0·0389
	(*b*) 10·0	28·21	19·50	0·0436
0·0450	(*a*) 20·0	19·27	2·32	0·0424
	(*b*) 20·0	34·09	16·06	0·0451
0·0519	(*a*) 10·0	12·7	2·99	0·0485
	(*b*) 10·0	21·45	11·08	0·05185
0·0652	(*a*) 10·0	14·70	2·89	0·05905
	(*b*) 10·0	21·40	8·37	0·06515
0·0778	15·0	41·84	18·05	0·0793

It is seen that, provided a sufficient excess of bromine solution be taken, indene can be estimated satisfactorily in carbon tetrachloride in concentrations up to 0·065M.

Effect of concentration on the rate of polymerisation of indene in carbon tetrachloride. The rate of polymerisation of indene in solution is very much slower than that of *cyclo*pentadiene. The results are given below of a series of experiments on the effect of concentration on the rate of polymerisation at 25° in carbon tetrachloride. Owing to the fact that polymerised indene reacts only very slowly with bromine, the actual amount of free indene in partially polymerised specimens is obtained directly from the results of titrations carried out after dilution, as described above.

C_9H_8 (g.-mols./l.) initially	0·0519	0·1000	0·4999	0·657	1·500	2·415
% polymerised in 24 hours	nil	nil	0·48	0·60	1·2	6·0

Peroxide effect in indene solutions: solutions made up in absence of air. All indene solutions made up as hitherto described showed the presence of peroxide when tested by Kharasch's method (*loc. cit.*). Solutions of indene in carbon tetrachloride were therefore made up in oxygen-free nitrogen with indene freshly distilled in pure nitrogen. Indene and carbon tetrachloride were distilled into a storage flask in the nitrogen, which was used to force out portions of the solution when required for analysis. The storage flask was not completely air-tight, as is shown by the results given in Table IV, where it is seen that after 90 hours sufficient oxygen had got in to give a positive test for peroxide; measurable change in the bromine titration value was not detectable until the next day. Data are added to show the behaviour of a solution made up in nitrogen as above but kept in contact with air.

TABLE IV.

	Stored in nitrogen.						In contact with air.		
Time (hours)	0	22	47	66	90	120	0	1·25	23
C_9H_8 (g.-mols./l.) ...	3·615	3·620	3·620	3·615	3·610	3·450	1·230	1·230	1·190
Peroxide test	–	–	–	–	+	++	–	+	++

Solutions of indene in pure acetonitrile (up to 4M) did not polymerise by more than 1% on keeping in stoppered bottles in contact with air for periods up to 14 days.

SUMMARY AND CONCLUSIONS.

It has been found (i) that *cyclo*pentadiene and indene can be estimated when diluted in carbon tetrachloride to an accuracy of 2—3% by the addition of bromine, also in carbon tetrachloride; (ii) that the polymerisation of *cyclo*pentadiene in carbon tetrachloride follows a bimolecular law, and that the polymerisation of indene under the same conditions is a much slower process; (iii) that the rate of polymerisation of each of these hydrocarbons in carbon tetrachloride is diminished by the addition of the antoxidant acetonitrile, and that no appreciable polymerisation occurs in pure acetonitrile, or in carbon tetrachloride when oxygen is excluded. It appears that polymerisation is connected with the formation of peroxide in the solutions of the hydrocarbons. It is therefore highly probable that the polymerisations of *cyclo*pentadiene and indene are processes involving autoxidation,

analogous to those known to occur in the case of acraldehyde and other similar substances (Moureu and Dufraisse, *Compt. rend.*, 1922, **174**, 258 : for other cases of autoxidational condensation, see " Considérations sur l'autoxydation," Institut international de chimie Solvay, 1926).

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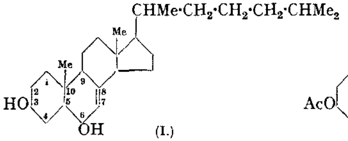
THE DYSON PERRINS LABORATORY, OXFORD. [*Received, March 31st*, 1937.]

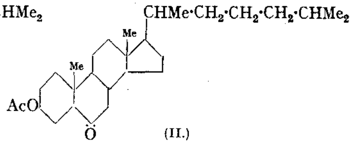
164. *Studies in the Sterol Group. Part XXXII. The Bromination of 6-Ketocholestanyl Acetate.*

By I. M. HEILBRON, E. R. H. JONES, and F. S. SPRING.

OF various alternative routes for the preparation of 7-dehydrocholesterol, one of the most promising appears to depend upon the accessibility of 3 : 6-dihydroxy-Δ^7-cholestene (I). With this general goal in view a study has been made of the bromination of 6-ketocholestanyl acetate (II).



(I.)



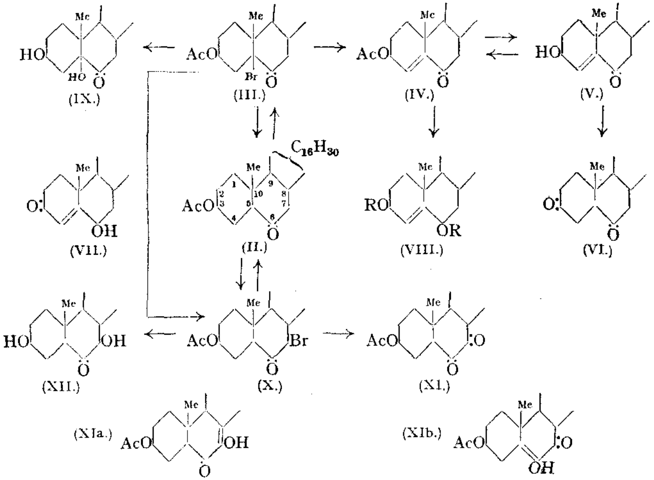
(II.)

Bromination of this saturated keto-acetate with one mole of bromine either in cold acetic acid, or in a mixture of acetic acid and ether at 0° or 35°, yields in each case a monobromide, m. p. 162° (decomp.). This has been characterised as *5-bromo-6-ketocholestanyl acetate* (III), since on treatment with pyridine it gives *6-keto-3-acetoxy-Δ^4-cholestene* (IV), which shows the typical light-absorption properties of an αβ-unsaturated ketone. Hydrolysis of the unsaturated keto-acetate (IV) with boiling methyl-alcoholic potash yields 3 : 6-diketocholestane (VI), identified both by a comparison with an authentic specimen and by the preparation of the dioxime. The formation of the saturated diketone is clearly dependent upon an isomerisation of the intermediate unsaturated alcohol (V), and offers a striking similarity to a reaction described recently by Butenandt and Schramm (*Ber.*, 1936, **69**, 2289), who obtained 3 : 6-diketocholestane instead of the anticipated 6-hydroxy-3-keto-Δ^4-cholestene (VII). On the other hand, Dane, Wang, and Schulte (*Z. physiol. Chem.*, 1936, **245**, 81) have isolated the ketol (VII) (as the semicarbazone) by hydrolysis of its acetate with cold 0·1*N*-methyl-alcoholic potash. We have similarly found that hydrolysis of 6-keto-3-acetoxy-Δ^4-cholestene (IV) with cold 0·2*N*-methyl-alcoholic potash gives *3-hydroxy-6-keto-Δ^4-cholestene* (V), m. p. 151°, characterised as an αβ-unsaturated ketone by its absorption spectrum; acetylation of (V) gives 6-keto-3-acetoxy-Δ^4-cholestene (IV). That the mechanism proposed for the formation of 3 : 6-diketocholestane from (IV) is correct is demonstrated by the fact that 3-hydroxy-6-keto-Δ^4-cholestene (V), *when heated* with alcoholic potash, is isomerised to 3 : 6-diketocholestane (VI).

An attempt was made further to characterise the unsaturated keto-acetate (IV) by converting it into the known 3 : 6-diacetoxy-Δ^4-cholestene (VIII; R = Ac) (Westphalen, *Ber.*, 1915, **48**, 1064). Reduction of 6-keto-3-acetoxy-Δ^4-cholestene (IV) with aluminium isopropoxide yielded an unsaturated diol (VIII; R = H), which gave a *diacetate*, m. p. 154—155°, and a *dibenzoate* (VIII; R = COPh), m. p. 198—199°. Since the former is not identical with the diacetate, m. p. 127°, described by Westphalen, the two must differ in the orientation of the groups associated with C_6.

Hydrolysis of 5-bromo-6-ketocholestanyl acetate (III) with alcoholic potash gives

3 : *5-dihydroxy-6-ketocholestane* (IX), m. p. 136° (*monobenzoate*, m. p. 170°). The presence of a tertiary hydroxyl group in (IX) is shown by its inability to form a dibenzoate, thus affording confirmation of the structure (III) allocated to the monobromide, m. p. 162°.



If the bromination of 6-ketocholestanyl acetate (II) be effected in acetic acid and ether at 35°, as previously described, and the reaction mixture then be heated under reflux for two hours, an isomeric monobromide, m. p. 145°, is produced to the exclusion of the compound, m. p. 162°. The bromination of (II) is dependent upon the presence of hydrogen bromide, since we find that the substitution reaction is completely inhibited by excess of potassium acetate and, further, that in many experiments the reaction can only be initiated by the addition of hydrogen bromide. Similar observations were made by Inhoffen (*Ber.*, 1936, **69**, 2141) in a study of the bromination of 3-keto-Δ^4-cholestene.

A survey of the conditions responsible for the preferential formation of the monobromides, m. p. 162° and 145°, has shown that the former is invariably the initial product and that, in the presence of hydrogen bromide, it is isomerised to the bromide, m. p. 145°. Confirmation of this mechanism was obtained in the observation that the monobromide, m. p. 162°, is converted into the lower-melting isomer on heating with hydrogen bromide in acetic acid. From this behaviour it was confidently anticipated that the two bromides would prove to be stereoisomers. With this in mind, unavailing attempts were made to convert the isomer, m. p. 145°, into 6-keto-3-acetoxy-Δ^4-cholestene (IV) by refluxing it either with pyridine, or with potassium acetate in alcoholic solution. Whereas treatment with silver nitrate and pyridine at room temperature or at 100° (Dane, Wang, and Schulte, *loc. cit.*) is similarly without effect, prolonged heating under reflux with this reagent gives a product, $C_{29}H_{46}O_4$, m. p. 156—157°, which has been characterised as 6 : 7-*diketocholestanyl acetate* (XI). Thus it produces an immediate green-violet coloration with ferric chloride and reacts with *o*-phenylenediamine, forming a *quinoxaline* derivative, m. p. 187°. 6 : 7-Diketocholestanyl acetate exhibits a broad band in the ultra-violet region of the spectrum with maximum at 2745 A.; it exists as the mono-enol modification (XIa or XIb), since the Zerewitinoff method indicates the presence of one active hydrogen atom. This extremely

facile oxidation of an α-bromo-ketone to an α-diketone is, we believe, due primarily to a *trans*-orientation of the halogen atom at C_7 relative to the hydrogen attached to C_8 and to the inherent reluctance to lose hydrogen bromide. The formation of an α-diketone from the bromide, m. p. 145°, can only be explained if the latter is *7-bromo-6-ketocholestanyl acetate* (X). This formulation has been confirmed by hydrolysis of the bromide to 3 : *7-dihydroxy-6-ketocholestane* (XII), m. p. 179°, which yields a *dibenzoate*, m. p. 169—170°, in contradistinction to the monobenzoate obtained from 3 : 5-dihydroxy-6-ketocholestane.

Butenandt and Wolff (*Ber.*, 1935, **68**, 2091) have shown that the orientation assumed by the halogen atom during the bromination of 3-ketocholane derivatives is dependent upon the stereochemical configuration of rings A and B; thus 3-ketocholestane gives a 2-bromo-substitution product, whereas 3-ketocoprostane is brominated exclusively at C_4. In marked contrast is the behaviour of 6-ketocholestanyl acetate, which can be brominated at either C_5 or C_7 according to the external conditions.

The metamorphoses of the various intermediates described in this paper are being further investigated together with the bromination of 7-ketocholestanyl acetate.

EXPERIMENTAL.

5-Bromo-6-ketocholestanyl Acetate (III).—(a) 6-Ketocholestanyl acetate (4·4 g.) in acetic acid (10 c.c.) and ether (50 c.c.) was treated with a solution of bromine in acetic acid (32 c.c.; 5%), added during 1 hour with stirring, the mixture being maintained at 0° throughout. Decolorisation proceeded rapidly, crystalline material separating after the addition of approximately half of the bromine solution. The ether was removed under reduced pressure, and the crystals collected and recrystallised from light petroleum (b. p. 60—80°), from which *5-bromo-6-ketocholestanyl acetate* (3·7 g.) separated in plates, m. p. 162° (decomp.; the m. p. varies with the rate of heating), $[\alpha]_D^{22°}$ − 133° (l = 1, c = 2·3 in chloroform). It is sparingly soluble in acetic acid and in light petroleum, but readily soluble in ether and in chloroform (Found: C, 66·3; H, 8·7. $C_{29}H_{47}O_3Br$ requires C, 66·5; H, 9·0%).

(b) 6-Ketocholestanyl acetate (1·0 g.) in ether (10 c.c.) was treated with a solution of bromine in chloroform (7·5 c.c.; 5%). The reaction, initiated by the addition of a drop of dilute hydrobromic acid, was complete in 10 minutes. The solvent mixture was removed in a stream of air, two crystallisations of the residue from acetic acid giving the monobromide, m. p. 162°.

7-Bromo-6-ketocholestanyl Acetate (X).—(a) 6-Ketocholestanyl acetate (5·5 g.) in acetic acid (12·5 c.c.) and ether (65 c.c.) was treated with a solution of bromine in acetic acid (40 c.c.; 5%) at 35°, the addition extending over 75 minutes. The mixture was then heated under reflux for 2 hours, the ether removed, and the solution set aside overnight at 15°. The hot solution was treated with water (5 c.c.) and the solid obtained on cooling was crystallised from aqueous acetic acid, *7-bromo-6-ketocholestanyl acetate* separating in lustrous plates, m. p. 144—145°, $[\alpha]_D^{22°}$ + 41° (l = 1, c = 1·7 in chloroform). From light petroleum the monobromide separates in hard prisms; it is moderately readily soluble in acetic acid and ethyl alcohol, very soluble in ether, chloroform and light petroleum (b. p. 60—80°), and in general considerably more soluble in the common organic solvents than the isomeric 5-bromo-6-ketocholestanyl acetate. It is moreover more stable than the latter, no decomposition occurring on heating to 220° (Found: C, 66·7; H, 8·6. $C_{29}H_{47}O_3Br$ requires C, 66·5; H, 9·0%).

(b) 5-Bromo-6-ketocholestanyl acetate (1·0 g.) in acetic acid (15 c.c.) was heated on the steam-bath for 15 minutes with a solution of hydrogen bromide in acetic acid (5 c.c.; 50%). The mixture showed a play of colour, passing through green to dark brown; after cooling, and the addition of water, the solution was seeded with the monobromide, m. p. 145°. The solid was collected and crystallised from dilute acetic acid, the 7-bromo-6-ketocholestanyl acetate (0·5 g.) obtained showing no depression in admixture with an authentic specimen. A solution of 5-bromo-6-ketocholestanyl acetate, treated in the same way but without the addition of hydrogen bromide, gave only the unchanged bromide.

Reduction of 7-Bromo- and 5-Bromo-6-ketocholestanyl Acetates.—A solution of each monobromide (1·0 g.) in ether was added to aluminium amalgam prepared from aluminium foil (5 g.) as described by Vogel (J., 1927, 594). The reaction mixture was treated with water from time to time during 36 hours, and the ether removed from the filtered liquid. After two crystallisations from methyl alcohol the residue gave 6-ketocholestanyl acetate, m. p. 127—128° either alone or in admixture with an authentic specimen.

6-Keto-3-acetoxy-Δ⁴-cholestene (IV).—5-Bromo-6-ketocholestanyl acetate (11·2 g.) in dry pyridine (90 c.c.) was heated under reflux for 8 hours. The mixture was diluted with ice-cold

water, and the solid collected and washed with water. After two crystallisations from methyl alcohol (charcoal), *6-keto-3-acetoxy-Δ^4-cholestene* (6·5 g.) separated in long hexagonal tables, m. p. 110°, $[\alpha]_D^{22^\circ}$ − 50·5° (l = 1, c = 1·1 in chloroform) (Found : C, 78·7; H, 10·6. $C_{29}H_{46}O_3$ requires C, 78·7; H, 10·5%). It gives a yellow coloration with tetranitromethane in chloroform solution; this is unusual for an αβ-unsaturated ketone. It is sparingly soluble in methyl alcohol but readily in pyridine. Light absorption in alcohol: Maxima, (a) 2360 A., log ε = 3·8; (b) 3200 A., log ε = 1·95.

3 : 6-*Diketocholestane*.—A solution of 6-keto-3-acetoxy-Δ^4-cholestene (1·0 g.) in methyl-alcoholic potassium hydroxide (30 c.c.; 4%) was heated under reflux for 1 hour. The cold solution was diluted with water, and the solid collected and washed with water. After crystallisation from ethyl acetate–alcohol (charcoal), followed by recrystallisation from acetone, 3 : 6-diketocholestane (0·5 g.) was obtained in needles, m. p. 169° either alone or in admixture with an authentic specimen (Found : C, 80·6; H, 10·9. Calc. for $C_{27}H_{44}O_2$: C, 80·9; H, 11·1%). The dioxime, m. p. 202°, showed no depression in admixture with an authentic specimen.

3-Hydroxy-6-keto-Δ^4-cholestene (V).—A solution of 6-keto-3-acetoxy-Δ^4-cholestene (IV) (1 g.) in methyl-alcoholic potassium hydroxide (100 c.c.; 1%) was set aside for 43 hours at room temperature. The mixture was largely diluted with water and acidified with dilute hydrochloric acid, and the product isolated by means of ether. After a single crystallisation from methyl alcohol (charcoal) *3-hydroxy-6-keto-Δ^4-cholestene* was obtained in short hard needles, m. p. 150—151°, $[\alpha]_D^{20^\circ}$ − 13° (l = 1, c = 2·8 in chloroform) (Found : C, 81·0; H, 11·1. $C_{27}H_{44}O_2$ requires C, 80·9; H, 11·1%). It is very soluble in methyl alcohol but insoluble in light petroleum. Light absorption in alcohol: Maxima, (a) 2390 A., log ε = 3·8; (b) 3190 A., log ε = 1·93.

Isomerisation of 3-Hydroxy-6-keto-Δ^4-cholestene (V) *to* 3 : 6-*Diketocholestane* (VI).—3-Hydroxy-6-keto-Δ^4-cholestene (100 mg.) in methyl-alcoholic potassium hydroxide (5 c.c.; 10%) was heated under reflux for 75 minutes. The solution was diluted with water, and the solid collected and washed with water. The crude product in methyl alcohol was decolorised with charcoal and, after removal of the solvent, taken up in acetone. Refrigeration effected the separation of a small quantity of a resinous solid. The decanted liquor was concentrated, and on cooling, 3 : 6-diketocholestane (20 mg.) separated which after one crystallisation from acetone showed no depression in m. p. in admixture with an authentic specimen.

3 : 6-*Diacetoxy-Δ^4-cholestene* (VIII, R = Ac).—Freshly distilled aluminium *iso*propoxide (5 g.) was added to a solution of 6-keto-3-acetoxy-Δ^4-cholestene in dry *iso*propyl alcohol (40 c.c.), and the mixture heated under reflux for 18 hours. The solvent was removed, the residue set aside for 50 minutes at 17° with a solution of methyl-alcoholic potassium hydroxide (50 c.c.; 6%), and the mixture largely diluted with water and extracted with ether. After drying (sodium sulphate), the solvent was removed, and the residual gum triturated with acetone to give a solid (1·1 g.), which separated from ethyl acetate in a micro-crystalline form, m. p. 178—179°. With the antimony trichloride reagent the diol gives an immediate pink coloration, changing to blue on standing. The diol (0·2 g.) was heated under reflux for 30 minutes with acetic anhydride (5 c.c.) and sodium acetate. Water was added to the hot solution, and the solid collected and washed with water. After two crystallisations from methyl alcohol 3 : 6-*diacetoxy-Δ^4-cholestene* separated in fine needles, which softened at 152°, m. p. 154—155°, clearing completely at 157°; $[\alpha]_D^{22^\circ}$ + 24·8° (l = 1, c = 1·0 in chloroform) (Found : C, 76·6; H, 10·5. $C_{31}H_{50}O_4$ requires C, 76·5; H, 10·4%). With the antimony trichloride reagent it slowly gives a sapphire-blue coloration.

3 : 6-*Dibenzoyloxy-Δ^4-cholestene* (VIII, R = COPh).—The diol (0·4 g.), m. p. 178—179°, in pyridine (1·8 c.c.) was set aside at room temperature for 18 hours with benzoyl chloride (0·6 c.c.). The addition of water precipitated a gum, which was triturated with methyl alcohol. Two crystallisations of the crude solid from chloroform–acetone gave the *dibenzoate* in small rectangular plates, m. p. 198—199°, clearing completely at 208°; $[\alpha]_D^{22^\circ}$ + 83·9° (l = 1, c = 1·8 in chloroform) (Found : C, 80·3; H, 8·7. $C_{41}H_{54}O_4$ requires C, 80·4; H, 8·9%). The dibenzoate is sparingly soluble in methyl alcohol and acetone, and very soluble in chloroform; with the antimony trichloride reagent it slowly gives a sapphire-blue coloration.

3 : 5-*Dihydroxy-6-ketocholestane* (IX).—5-Bromo-6-ketocholestanyl acetate (1·0 g.) was heated under reflux with methyl-alcoholic potash (30 c.c.; 10%) for 2 hours. After dilution with water the resinous product was isolated by means of ether and taken up in hot methyl alcohol, and the solution cooled. The clear solution was decanted from the separated gum, diluted with water, and set aside at 0°; a yellow solid (0·6 g.) separated which after two crystallisations from methyl alcohol (charcoal) gave 3 : 5-dihydroxy-6-ketocholestane in rectangular tables, softening at 128°, m. p. 138°, $[\alpha]_D^{22^\circ}$ + 29·3° (l = 1, c = 2·2 in chloroform). It is spar-

ingly soluble in methyl alcohol but very soluble in chloroform and pyridine. The diol separates with solvent of crystallisation which cannot be completely removed even after prolonged desiccation. The *monobenzoate*, prepared by the action of benzoyl chloride (0·25 c.c.) on the diol (150 mg.) in excess of pyridine at room temperature for 15 hours, separates from methyl alcohol–acetone either in long fine needles or in soft plates, the two forms being interconvertible; m. p. 170°, $[\alpha]_D^{20°}$ + 23·0° (l = 1, c = 0·8 in chloroform). It is very sparingly soluble in methyl alcohol but readily soluble in acetone (Found: C, 78·3; H, 9·7. $C_{34}H_{50}O_4$ requires C, 78·1; H, 9·7%).

6 : 7-*Diketocholestanyl Acetate* (XI).—A solution of 7-bromo-6-ketocholestanyl acetate (1·0 g.) and silver nitrate (2 g.) in pyridine (20 c.c.) was heated under reflux for 5 hours. Ether was added to the cold solution, and the mixture washed with dilute sulphuric acid and water. After drying and evaporation a red-brown gum was obtained, which was taken up in hot alcohol (charcoal). The solid (160 mg.) separating on cooling was recrystallised from methyl alcohol to give 6 : 7-*diketocholestanyl acetate* in fine hard needles, m. p. 156—157°, $[\alpha]_D^{20°}$ − 108° (l = 1, c = 1·0 in chloroform) (Found: C, 76·0; H, 9·8. $C_{29}H_{46}O_4$ requires C, 75·9; H, 10·1%). It is freely soluble in dilute aqueous-alcoholic sodium hydroxide to give a yellow solution, from which it is precipitated by acidification. With alcoholic ferric chloride, an immediate green-violet coloration is produced. Active hydrogen determination (Zerewitinoff): The diketone (8·12 mg.) evolved 0·48 c.c. of methane at 18° and 757 mm., corresponding to 1·1 atoms of active hydrogen per mole. Light absorption in alcohol: Maximum, 2745 A., log ε = 4·03.

Quinoxaline Derivative of 6 : 7-*Diketocholestanyl Acetate.*—The diketone (100 mg.) was fused with *o*-phenylenediamine (100 mg.) for 40 minutes at 140—150°. The dark brown mass solidified on cooling; it was crystallised from ethyl acetate, and the product (35 mg.) recrystallised from acetone, from which the *quinoxaline* derivative separated in colourless hair-like needles, m. p. 186—187° (Found: C, 79·4; H, 9·7. $C_{35}H_{50}O_2N_2$ requires C, 79·2; H, 9·4%).

3 : 7-*Dihydroxy*-6-*ketocholestane* (XII).—A solution of 7-bromo-6-ketocholestanyl acetate (2·3 g.) in methyl-alcoholic potassium hydroxide (70 c.c.; 10%) was heated under reflux for 2 hours. After dilution with water the resinous product was isolated by means of ether and dissolved in methyl alcohol. On cooling and decantation from resin, a mass of yellow needles (1·1 g.) separated, which after two crystallisations from methyl alcohol (charcoal) formed lustrous plates, m. p. 179°, $[\alpha]_D^{23°}$ + 31·4° (l = 1, c = 1·0 in chloroform). 3 : 7-*Dihydroxy*-6-*ketocholestane* is sparingly soluble in methyl alcohol, soluble in acetone, and very soluble in chloroform and pyridine (For analysis the specimen was dried in a vacuum at 100° for 8 hours. Found: C, 77·2; H, 11·0. $C_{27}H_{46}O_3$ requires C, 77·4; H, 11·1%). The keto-diol sublimes unchanged in needles at 220°/10^{-3} mm., whereas the isomeric 3 : 5-dihydroxy-6-ketocholestane suffers profound decomposition under similar conditions. The *dibenzoate*, prepared by treatment of the keto-diol (120 mg.) in excess of pyridine with benzoyl chloride (0·17 c.c.) for 20 hours at room temperature, separates from methyl alcohol–acetone in long hard needles, m. p. 169—170°, $[\alpha]_D^{20°}$ + 62·0° (l = 1, c = 1·0 in chloroform). It is sparingly soluble in methyl alcohol but very soluble in acetone (Found: C, 78·7; H, 8·7. $C_{41}H_{54}O_5$ requires C, 78·5; H, 8·7%).

Our thanks are due to the Rockefeller Foundation for a grant and to the University of Wales for a Fellowship to one of us (E. R. H. J.).

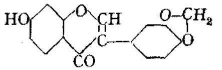
The University, Manchester. [*Received, March 4th*, 1937.]

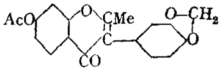
165. *Synthetical Experiments in the* iso*Flavone Group. Part VIII. Note on ψ-Baptigenin.*

By Wilson Baker, Robert Robinson, and N. M. Simpson.

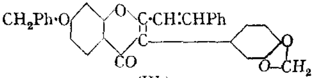
ψ-Baptigenin (I), the aglucone of ψ-baptisin (Gorter, *Arch. Pharm.*, 1897, **235**, 494; Späth and Schmidt, *Monatsh.*, 1929, **53**, 454), has been synthesised by Späth and Lederer (*Ber.*, 1930, **63**, 743), who employed the cyanohydrin method introduced in Part V of this series (Baker, Pollard, and Robinson, J., 1929, 1468). ψ-Baptigenin has also been synthesised by Mahal, Rai, and Venkataraman (J., 1934, 1771), who used a method for the construction of the chromone nucleus (condensation of an *o*-hydroxyacetophenone derivative with ethyl formate in the presence of sodium) which was first employed by Perkin and

Robinson in the synthesis of anhydrobrazilic acid (J., 1908, **93**, 509). The synthesis herein described (much delayed in publication) is therefore only of interest as an example of the modification of one of the methods available in the series such that phenolic representatives containing groups sensitive to dealkylating agents can be obtained. As in many analogous cases, we have adopted the device of benzylation of the hydroxyl group which must eventually be selectively regenerated from the ether. Protection of this phenolic hydroxyl group is necessary at the stage of the permanganate oxidation (*v. infra*).

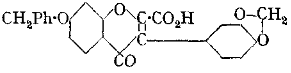
(I.) 

 (II.)

ω-Piperonylresacetophenone (ψ-baptigenetin) (Späth and Schmidt, *loc. cit.*) is synthesised by means of the Hoesch reaction and converted by heating with acetic anhydride and sodium acetate into *7-acetoxy-3′ : 4′-methylenedioxy-2-methyl*iso*flavone* (II). This substance is hydrolysed, benzylated, and condensed with benzaldehyde, forming *7-benzyloxy-3′ : 4′-methylenedioxy-2-styryl*iso*flavone* (III). This is oxidised at the styryl group to *7-benzyloxy-3′ : 4′-methylenedioxy*iso*flavone-2-carboxylic acid* (IV). When this acid is heated with acetic and hydrobromic acids, ψ-baptigenin identical with the natural product is obtained; debenzylation and decarboxylation are thus effected in one operation. We are greatly indebted to Prof. E. Späth for the provision of a specimen of the *iso*flavone of natural origin.



(III.)



(IV.)

Experimental.

*7-Acetoxy-3′ : 4′-methylenedioxy-2-methyl*iso*flavone* (II).—A mixture of ω-piperonylresacetophenone (32 g.), acetic anhydride (110 c.c.), and sodium acetate (28 g.) was refluxed (bath at 180°) for 24 hours, the product mixed with dilute hydrochloric acid, and the solid collected (30 g.). The *isoflavone* crystallised from alcohol in elongated, colourless prisms, m. p. 198·5° after sintering from 195° (Found: C, 67·2; H, 4·2. $C_{19}H_{14}O_6$ requires C, 67·5; H, 4·2%). It is moderately readily soluble in hot alcohol.

*7-Hydroxy-3′ : 4′-methylenedioxy-2-methyl*iso*flavone*.—This homologue of ψ-baptigenin, readily obtained by the hydrolysis of the foregoing acetate with aqueous alcoholic potassium hydroxide on the steam-bath, crystallised from alcohol in colourless, rectangular plates, m. p. 253—254·5° after sintering at 244° (Found: C, 68·7; H, 4·2. $C_{17}H_{12}O_5$ requires C, 68·9; H, 4·1%), readily soluble in hot alcohol.

Benzyl Ether.—A mixture of homo-ψ-baptigenin (7·5 g.), anhydrous sodium carbonate (7·5 g.), sodium iodide (0·5 g.), and acetone (100 c.c.) was refluxed and stirred for 12 hours while benzyl chloride (4·5 g.) was gradually added. The operation was continued for 24 hours more and the product was then precipitated by the addition of water. The solid was collected, washed with water and alcohol, dried (7 g.), and crystallised from alcohol, being so obtained in long, colourless needles, m. p. 186° (Found: C, 74·2; H, 4·7. $C_{24}H_{18}O_5$ requires C, 74·6; H, 4·7%). The *ether* is sparingly soluble in hot alcohol and readily soluble in warm acetic acid.

*7-Benzyloxy-3′ : 4′-methylenedioxy-2-styryl*iso*flavone* (III).—Benzaldehyde (2·8 g.) was added to a mixture of benzyloxymethylenedioxymethyl*iso*flavone (7 g.) and alcoholic sodium ethoxide (0·5 g. of sodium in 100 c.c.), which was then refluxed for 1 hour. After a few hours the solid was collected and extracted with hot alcohol (50 c.c.), and the insoluble portion crystallised from acetic acid (yield, 6 g.). Recrystallised from acetic acid, the *isoflavone* formed clusters of pale yellow, microscopic prisms, m. p. 199—200·5° (Found: C, 78·5; H, 4·7. $C_{31}H_{22}O_5$ requires C, 78·5; H, 4·7%), very sparingly soluble in hot alcohol and readily soluble in hot acetic acid.

Condensation of benzyloxymethylenedioxy-2-methyl*iso*flavone with nitrosodimethylaniline could not be effected. An analogous series of experiments with 7 : 4′-dimethoxy-2-methyl*iso*flavone was also fruitless.

7-Benzyloxy-3′ : 4′-methylenedioxyisoflavone-2-carboxylic Acid (IV).—A solution of potassium permanganate (10 g.) in water (200 c.c.) was fairly quickly added to one of benzyloxymethylenedioxystyryl*iso*flavone (8·3 g.) in pure pyridine (300 c.c.). Complete reduction of the permanganate occurred in 20 minutes and 5% permanganate solution (100 c.c.) was then added slowly with stirring during 2 hours. The liquid was heated to boiling, filtered, and mixed with water and an excess of hydrochloric acid. The precipitate was collected, triturated with 50% acetic acid, collected, and crystallised from 90% acetic acid and then from glacial acetic acid (yield, 3·7 g.). The *acid* crystallises from acetic acid (great disparity between solubilities in hot and cold), in pale ochreous needles and from acetone in nearly colourless, stout, microscopic needles, m. p. 179—181° (Found : C, 69·0; H, 3·9. $C_{24}H_{16}O_7$ requires C, 69·2; H, 3·8%). The acid is readily soluble in aqueous sodium carbonate; it is decarboxylated on heating above its m. p. and the product is *O*-benzyl-ψ-baptigenin, m. p. 167° (cf. Mahal, Rai, and Venkataraman, *loc. cit.*).

ψ-Baptigenin (I).—The foregoing carboxylic acid (0·6 g.) was dissolved in boiling acetic acid (10 c.c.), and hydrobromic acid (10 c.c., *d* 1·5) added. The clear solution was raised to the b. p. and then heated in boiling water for 1 hour. The odour of benzyl bromide became apparent and, as a test showed that the products were much more soluble than had been anticipated, the liquid was diluted with ether and washed with water. The green fluorescence of the aqueous solution was greatly enhanced when it was neutralised with sodium carbonate and a milkiness was produced. Eventually a small sandy precipitate was obtained and this was collected centrifugally and combined with the material obtained from the ethereal solution. The latter was washed with aqueous sodium carbonate until the washings were distinctly alkaline and then once again; acidification of this extract afforded no precipitate. Aqueous sodium hydroxide, however, extracted ψ-baptigenin, which was obtained in a crude condition by acidification of the solutions. The material, sublimed in a high vacuum (bath at 220°) and crystallised from alcohol, formed colourless needles, m. p. 293—294° (decomp.). The m. p. was not depressed by admixture with an authentic specimen of natural origin. Direct comparison of the behaviour towards solvents and reagents disclosed no divergence of properties and the crystalline habit was identical in the case of the two specimens.

Dyson Perrins Laboratory, Oxford University. [*Received, March 25th*, 1937.]

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166. *The Coupling of Diazonium Salts with Derivatives of Cyclic β-Ketonic Acids.*

By R. P. Linstead and Abel Bao-Lang Wang.

Fifty years ago, Japp and Klingemann found that benzenediazonium chloride coupled with ethyl methylacetoacetate in alkaline solution to give the phenylhydrazone of ethyl pyruvate with elimination of acetic acid; if, on the other hand, the ketonic ester was first hydrolysed by standing with alkali and then coupled, the product was the monophenylhydrazone of diacetyl, carbon dioxide being eliminated (*Ber.*, 1887, **20**, 2942, 3284, 3398; *Annalen*, 1888, **247**, 190) :

$$\text{(i)}\ CH_3{\cdot}CO\vdots CHMe{\cdot}CO_2Et \longrightarrow CH_3{\cdot}CO_2H + CH_3{\cdot}C(CO_2Et){:}N{\cdot}NHPh$$

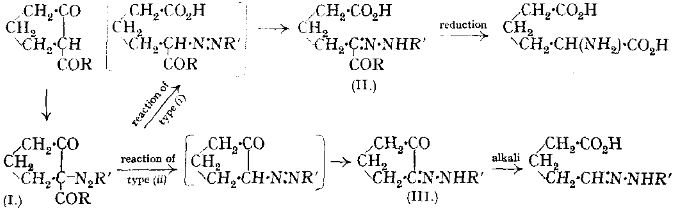
$$\text{(ii)}\ CH_3{\cdot}CO{\cdot}CHMe\vdots CO_2Na \longrightarrow CH_3{\cdot}CO{\cdot}CMe{:}N{\cdot}NHPh + CO_2$$

These reactions resemble the acidic and ketonic fissions of β-ketonic esters.

Dieckmann obtained a parallel to reaction (ii) in the alicyclic series by preparing *cyclo*pentane-1 : 2-dione monophenylhydrazone from ethyl *cyclo*pentanone-2-carboxylate (*Annalen*, 1901, **317**, 27), a process which has been extended by Lions (*J. Proc. Roy. Soc. N. S. Wales*, 1932, **66**, 516). Reaction (i), which now involves a fission of the ring, was realised for alicyclic compounds independently by Kalb, Schweizer, and others (*Ber.*, 1926, **59**, 1858, 1860) and by Manske and Robinson (J., 1927, 240; compare Jackson and Manske, *J. Amer. Chem. Soc.*, 1930, **52**, 5209). This modification is of particular interest in connection with the synthesis of physiologically important indole derivatives. We have made a general investigation of the reaction of diazonium salts with derivatives of cyclic β-ketonic

acids, with the object of determining the mechanism of these two degradations which follow the coupling reaction. In the summary which follows, we shall refer only to the compounds obtained from benzenediazonium chloride, except where other diazonium salts gave substances of special interest.

The structures of the products obtained from ethyl *cyclo*pentanone-2-carboxylate by the two processes were first confirmed. When coupling immediately followed the dissolution of the ester in alkali, the main product was ethyl hydrogen α-ketoadipate phenylhydrazone (II; R = OEt, R′ = Ph), the structure of which followed from its conversion into α-aminoadipic acid by reduction and hydrolysis. A small amount of *cyclo*pentane-1 : 2-dione monophenylhydrazone (III, R′ = Ph) was formed in this coupling. The nature of this was proved by its conversion into the corresponding osazone, which was independently synthesised. Similar dione monophenylhydrazones were the sole products when the keto-ester was first allowed to stand with alkali and then coupled. These products are insoluble in aqueous alkali, but alcoholic potash causes ring fission. Thus, cyclo*pentane*-1 : 2-*dione mono*-o-*nitrophenylhydrazone* (III, R′ = $C_6H_4{\cdot}NO_2$) yielded the o-*nitrophenylhydrazone of* ω-*aldehydovaleric acid*.



By coupling 2 : 4-dinitrobenzenediazonium sulphate with *cyclo*pentanonecarboxylic ester in acetic acid, the intermediate *azo-ester* [I; R = OEt, R′ = $C_6H_3(NO_2)_2$] was isolated. This was very unstable to alkali, the ring being broken even by cold aqueous sodium carbonate to yield the 2 : 4-*dinitrophenylhydrazone* of *ethyl hydrogen* α-*ketoadipate* [II; R = OEt, R′ = $C_6H_3(NO_2)_2$]. From this were prepared the corresponding *di-ester*, *di-acid*, and α-aminoadipic acid. Kalb, Schweizer, Zellner, and Berthold (*Ber.*, 1926, **59**, 1863) describe the preparation of a similar azo-ester by coupling *p*-nitrobenzenediazonium chloride with the same keto-ester in aqueous sodium acetate, but we were never able to isolate azo-esters from couplings in aqueous media.

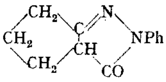
When *cyclo*pentanone-2-carboxyanilide was used in place of the ester as the second component, the same dione hydrazones (type III) were isolated, but the principal products were azo-anilides * (type I; R = NHPh, R′ = substituted phenyl). These azo-anilides were stable to cold aqueous alkali, and were in fact prepared in this medium. Dieckmann (*loc. cit.*) was unable to obtain 1-*phenyl*-3 : 4-cyclo*pentano*-5-*pyrazolone* (IV), but this has now been prepared, although in such poor yield that its coupling with diazonium salts was not investigated.

These reactions were paralleled in the *cyclo*hexane series. In this case an intermediate *azo-ester* (V) was isolated by coupling *p*-nitrobenzenediazonium sulphate with ethyl *cyclo*hexane-2-one-1-carboxylate in acetic acid.

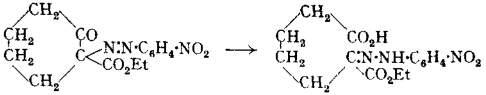
This on treatment with sodium carbonate gave the p-*nitrophenylhydrazone* of *ethyl hydrogen* α-*ketopimelate* (VI), identical with material obtained by direct coupling in alkali. Hydrolysis and reduction of (VI) yielded α-aminopimelic acid. As in the homologous series, the *azo-anilide* corresponding to (V) was stable and showed no tendency to ring fission. The hydrolysis of these azo-esters yields only products corresponding to an acidic fission and

* These are the cyclic analogues of the technically valuable "Hansa Yellows" (for which see Rowe, Burr, and Corbishley, *J. Soc. Dyers and Col.*, 1926, **42**, 80; Burr and Rowe, *ibid.*, 1928, **44**, 205; Fierz-David and Ziegler, *Helv. Chim. Acta*, 1928, **11**, 776).

not to a ketonic fission, even when very weak alkali is used. This falls into line with the fact that substited β-ketonic esters are hydrolysed by weak alkali to ketones only when the



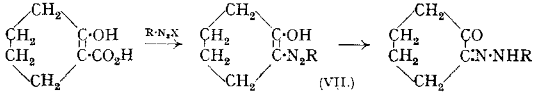
(IV.)



(V.) (VI.)

substituents are small alkyl groups. When the substituent groups are large or negative, acids are the almost exclusive fission products (Fittig, Claisen). These decompositions of azo-esters establish the mechanism of reactions of type (i).

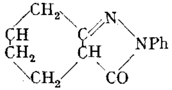
It was next necessary to justify the hypothesis that it is the free ketonic acid, formed by preliminary hydrolysis, which yields the diketone monohydrazone (reaction ii). When pure *cyclo*hexanone-2-carboxylic acid was treated with diazonium salts, even in acetic acid solution, no azo-acid could be isolated: carbon dioxide was at once evolved and the products were dione monohydrazones (VII). The reaction recalls the coupling of *p*-hydroxybenzoic acid with diazonium salts, in which the carboxyl group is eliminated.

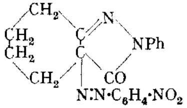


(VII.)

In interesting contrast to the *cyclo*pentane analogue, 1-phenyl-3 : 4-*cyclo*hexano-5-pyrazolone (VIII) is obtainable in excellent yield (compare Dieckmann, *loc. cit.*, p. 45). The difference between the ease of formation of the two dicyclic pyrazolones (IV and VIII) is attributable to the strain in the *cyclo*pentane derivative. The double bond must lie at a bridge head, or possibly in the bridge itself. This can be tolerated in the *cyclo*hexane derivative with little divergence from the tetrahedral arrangement, but the *cyclo*pentane compound is much more strained.

(VIII.)





(IX.)

The pyrazolone (VIII) coupled readily with *p*-nitrobenzenediazonium sulphate in acetic acid. The azo-pyrazolone (IX) could not be isolated in a pure condition, but its presence in the product could be deduced from two striking decompositions. Owing to the stabilisation of the alicyclic ring by the locking in the dicyclic system the general instability associated with structures of type I (or IX) now revealed itself in the ease with which the azo-group was eliminated. Digestion of the reaction product with alcohol regenerated the pyrazolone (VIII) and formed acetaldehyde, nitrobenzene, and nitrogen :

$$R{\cdot}N{:}N{\cdot}C_6H_4{\cdot}NO_2 + C_2H_5{\cdot}OH \longrightarrow RH + N_2 + C_6H_5{\cdot}NO_2 + CH_3{\cdot}CHO$$

Treatment of (IX) with dimethylaniline in acid yielded *p*-nitrobenzeneazodimethylaniline, a reaction which must be presumed to involve the reversal of the ordinary coupling reaction at an intermediate stage.

EXPERIMENTAL.

cyclo*Pentane Series.*

Intermediates.—The yield of *cyclo*pentanone-2-carboxyanilide obtained from the ester following Blount, Perkin, and Plant (J., 1929, 1983) was 50%. The following process, based on that of Fierz-David and Ziegler for acetoacetic arylamides (*loc. cit.*), gave a 75—80% yield of an iden-

tical product. To a mixture of 156 g. of the keto-ester, 300 c.c. of xylene, and 3 c.c. of pyridine at 130—140°, a mixture of 93 g. of aniline, 200 c.c. of xylene, and 2 c.c. of pyridine was added during 3 hours. After a further 2 hours at the same temperature, the solvent was removed under reduced pressure, the residue shaken with 1 l. of 4% aqueous sodium hydroxide, and the solution filtered from the insoluble anil-anilide (below) and acidified with dilute acetic acid. The keto-anilide, isolated by means of ether, crystallised from light petroleum in plates (150 g.), m. p. 103·5—104° (Found: C, 70·8; H, 6·5. Calc.: C, 70·9; H, 6·4%). The anilide is soluble in dilute sodium hydroxide and insoluble in dilute sodium carbonate solution. Concentrated aqueous sodium hydroxide precipitates the sodium salt.

The insoluble product from the above reaction was washed with dilute acid and water and crystallised from alcohol. The *anil* of cyclo*pentanone-2-carboxyanilide* formed colourless prisms, m. p. 128—130° (Found: C, 77·9; H, 6·2. $C_{18}H_{18}ON_2$ requires C, 77·7; H, 6·4%). The third possible product from the interaction of these reagents, namely, the anil of the keto-ester, was described by Blount, Perkin, and Plant (*loc. cit.*) as an oil. A mixture of 10 g. of the keto-ester, 6 g. of aniline, and a drop of acetic acid was kept over alkali in a desiccator for 10 days. The residue was scratched with light petroleum (b. p. 40—60°) at − 15° and quickly pressed on a tile. The solid on recrystallisation yielded the *anil* of *ethyl* cyclo*pentanone-2-carboxylate* in large prisms, m. p. 58·5° (Found: C, 72·7; H, 7·1. $C_{14}H_{17}O_2N$ requires C, 72·7; H, 7·3%).

*Bis*cyclo*pentanone-2-carboxybenzidide* was prepared in the same way as the corresponding anilide. The product was repeatedly extracted with a 2% solution of sodium hydroxide in 30% alcohol, in which it dissolved slowly, and reprecipitated with acetic acid until it was white (Found: C, 71·1; H, 5·9; ash, 0·2. $C_{24}H_{24}O_4N_2$ requires C, 71·4; H, 5·9%). It did not melt below 250°.

1-*Phenyl*-3 : 4-cyclo*pentano-5-pyrazolone* (IV).—A mixture of ethyl *cyclo*pentanone-2-carboxylate (10 g.), phenylhydrazine (10 g.), acetic acid (5 c.c.), and a few drops of sulphuric acid was heated for 16 hours on a steam-bath. The residue was poured into 100 c.c. of ether and extracted thrice with 50 c.c. portions of 2*N*-hydrochloric acid. (The ethereal layer yielded the phenylhydrazone of the keto-ester, m. p. 90·5°, in agreement with Dieckmann; *loc. cit.*) The acid layer was made alkaline and extracted with ether. The alkaline solution was carefully acidified with acetic acid, and the small amount of voluminous precipitate was filtered off, separated from tarry matter, and crystallised from 50% alcohol. The *pyrazolone* separated in lustrous needles (10 mg.), m. p. 177—178° (Found: C, 71·9; H, 5·9; N, 14·2. $C_{12}H_{12}ON_2$ requires C, 72·0; H, 6·0; N, 14·0%), sparingly soluble in organic solvents and soluble both in acid and in alkali. Attempts to prepare the pyrazolone by cyclising the corresponding phenylhydrazone were unsuccessful.

Coupling Reactions.—(i) *Ester*. A solution of aniline (10 g.) in hydrochloric acid (20 c.c.) and ice-water (30 c.c.) was diazotised with a solution of 7 g. of sodium nitrite in 50 c.c. of water, and 10 g. of sodium acetate were added. The mixture was added slowly at 0° with stirring to a fresh solution of ethyl *cyclo*pentanone-2-carboxylate (16 g.) in 2·5% aqueous sodium hydroxide (400 c.c.). The brownish-red precipitate of *cyclo*pentane-1 : 2-dione monophenylhydrazone (III, R′ = Ph) was collected after 16 hours and crystallised from alcohol, giving 1 g. of yellow-orange plates, m. p. 201—203° (decomp.), soluble in caustic alkali to give a green solution, insoluble in sodium carbonate (Found: C, 70·1; H, 6·4. Calc.: C, 70·2; H, 6·4%). The mother-liquor on the addition of sodium chloride gave a semi-solid sodium salt, yielding a red oil on acidification. This was purified through sodium carbonate and then solidified on long standing. Crystallisation from benzene yielded ethyl hydrogen α-ketoadipate phenylhydrazone (II; R = OEt, R′ = Ph), m. p. 120° (compare Kalb *et al.*, *loc. cit.*). On hydrolysis with cold alcoholic potash this yielded the corresponding acid, m. p. 141°, in agreement with Gault (*Bull. Soc. chim.*, 1912, **11**, 387). The acid so prepared from 4 g. of the half-ester was reduced with tin (10 g.) and warm hydrochloric acid (50 c.c.) until colourless. After dilution to 200 c.c. the tin was removed by means of hydrogen sulphide, and the filtrate basified and evaporated. Aniline was identified in the distillate as the tribromo-derivative. α-Aminoadipic acid, isolated from the residue through the copper salt, had m. p. 205—206°.

The dione monophenylhydrazone described above was converted by means of phenylhydrazine in alcoholic acetic acid into the corresponding osazone, which formed brownish-yellow needles (from alcohol), m. p. 144°. The same substance (m. p. and mixed m. p.) was obtained by the action of alcoholic phenylhydrazone on *cyclo*pentane-1 : 2-dione, prepared (1·5 g., b. p. 117°/18 mm.) by oxidizing 25 g. of *cyclo*pentanone with 28 g. of selenium dioxide, following Riley, Morley, and Friend (J., 1932, 1898).

Using *o*- or *p*-nitroaniline in place of aniline in the above process, we were unable to obtain

solid half-ester hydrazones; but the corresponding dione hydrazones were readily made in good yields by the following procedure, a modification of that of Lions (*loc. cit.*). Ethyl *cyclo*pentanone-2-carboxylate (8 g.) was kept for 16 hours at 0° with a solution of sodium hydroxide (2·2 g.) in 50% alcohol (100 c.c.). Diazotised *p*-nitroaniline (7 g. of base) was added in one portion, and the mixture stirred with 10 g. of sodium acetate. After 20 minutes the gummy product was collected and washed.

cyclo*Pentane*-1 : 2-*dione mono*-p-*nitrophenylhydrazone* (III; R' = $C_6H_4{\cdot}NO_2$) crystallised on standing, and separated from alcohol in yellow needles, m. p. 242°. It is insoluble in sodium carbonate; the solution in sodium hydroxide is blood-red (Found : C, 56·3; H, 4·7. $C_{11}H_{11}O_3N_3$ requires C, 56·6; H, 4·6%). The corresponding *mono-o-nitrophenylhydrazone*, prepared similarly from *o*-nitroaniline, is dimorphous. When crystallised from acetic acid, it forms long golden-yellow needles, unchanged on being dried in a vacuum desiccator (Found : C, 56·6; H, 4·7%). When the yellow form, contaminated with a trace of acetic acid, is dried at 100°, it changes completely into stout orange needles; but is unchanged if first dried and then heated to 100°. Both forms, and a mixture of the two, melt at 176—177° (slow heating) or 172—177° (rapid heating).

Ring fission. *cyclo*Pentane-1 : 2-dione mono-*o*-nitrophenylhydrazone (2 g.) was kept with an excess of aqueous alcoholic potassium hydroxide. The dark red solution deposited a brown precipitate, which changed to yellow crystals. After 5 days the mixture was diluted and acidified; the acidic product was purified through sodium bicarbonate and crystallised from acetone–light petroleum. ω-*Aldehydovaleric acid* o-*nitrophenylhydrazone* formed thin yellow needles (0·8 g.), m. p. 170—172° (Found : C, 52·6; H, 5·1. $C_{11}H_{13}O_4N_3$ requires C, 52·5; H, 5·2%).

6 C.c. of sulphuric acid were added to a solution of 9·2 g. of 2 : 4-dinitroaniline in hot acetic acid (60 c.c.), the mixture quickly cooled to 15°, and 9 c.c. of butyl nitrite added with stirring below 20° (cf. Hantzsch, *Ber.*, 1901, **34**, 3337). The diazonium salt was precipitated with 200 c.c. of ether, washed with ether, and redissolved in 50 c.c. of acetic acid. To the solution was added ethyl *cyclo*pentanonecarboxylate (10 c.c.) in acetic acid (50 c.c.), followed by sodium acetate (10 g.). After 16 hours, water precipitated 12 g. of crude azo-ester. Three crystallisations from 50% acetic acid yielded 5 g. of *ethyl* 2-(2' : 4'-*dinitrobenzeneazo*)cyclo*pentanone-2-carboxylate* [I; R = OEt, R' = $C_6H_3(NO_2)_2$] in lustrous, light yellow needles, m. p. 162—164° (decomp.), insoluble in sodium bicarbonate, soluble with difficulty in sodium carbonate, readily soluble in sodium hydroxide solution with a blood-red colour (Found : C, 47·7; H, 4·2. $C_{14}H_{14}O_7N_4$ requires C, 48·0; H, 4·0%).

Acidic fission of the azo-ester. 5 G. of the above compound were shaken in the cold with 200 c.c. of 2% aqueous sodium carbonate and 50 c.c. of ether until carbon dioxide was no longer evolved. The ethereal layer was separated and acidified with hydrochloric acid, and the yellow precipitate taken up in more ether and purified through sodium bicarbonate solution. Removal of ether and crystallisation from benzene and ethyl acetate yielded *ethyl hydrogen α-ketoadipate* 2 : 4-*dinitrophenylhydrazone* [II; R = OEt, R' = $C_6H_3(NO_2)_2$] in yellow needles (4 g.), m. p. 168—170° (decomp.), moderately easily soluble in alcohol and ether, soluble in acetone, appreciably soluble in water (deep yellow solution) and readily soluble in sodium bicarbonate (orange solution). It could be titrated with $N/10$-baryta, acting as a self-indicator, but the end-point was not sharp (Found : C, 45·2; H, 4·3. $C_{14}H_{16}O_8N_4$ requires C, 45·6; H, 4·3%). The presence of the carbethoxy-group was proved by hydrolysis of 2 g. with 5% sodium hydroxide solution and fractional distillation. Ethyl alcohol in the final distillate was identified as the 3 : 5-dinitrobenzoate by Henstock's method (J., 1933, 216). For the isolation of the acid, 4 g. of the half-ester were kept with 1·5 g. of potassium hydroxide in 80% alcohol (60 c.c.) for 3 days. The acid was isolated by means of ether and purified through sodium bicarbonate and by crystallisation from water (once) and acetone (twice). *α-Ketoadipic acid* 2 : 4-*dinitrophenylhydrazone* formed powdery yellow crystals (2 g.), m. p. 238—240° (decomp.). The acid was sparingly soluble in organic solvents, and gave a deep yellow solution in water, turned brown by alkali. It gave approximately the correct equivalent on titration, acting as a self-indicator (Found : C, 42·4; H, 3·6. $C_{12}H_{12}O_8N_4$ requires C, 42·4; H, 3·5%). Esterification of the half-ester at room temperature by the Fischer–Speier method yielded the *diethyl* ester, which slowly solidified and formed lemon-yellow needles from light petroleum, m. p. 48—50° (Found : C, 48·1; H, 5·3. $C_{16}H_{20}O_8N_4$ requires C, 48·5; H, 5·2%). It yielded the di-acid hydrazone on hydrolysis. 3 G. of the di-acid hydrazone were reduced by the procedure already described, except that the aromatic reduction product (triaminobenzene) was removed by extraction with chloroform instead of distillation in steam. The acidic product was α-aminoadipic acid, identical with that already isolated.

(ii) *Anilide and benzidide.* The diazonium chloride prepared from 13·8 g. of *p*-nitroaniline and 35·5 c.c. of concentrated hydrochloric acid was treated with 10 g. of sodium acetate, and dropped into an ice-cooled, stirred solution of 20·2 g. of *cyclo*pentanone-2-carboxyanilide in 500 c.c. of 3% aqueous sodium hydroxide. A yellow precipitate at once separated from the purple solution. After 2 hours the product was acidified (to assist filtration), and the orange solid filtered off and shaken with 2% sodium hydroxide solution (500 c.c.). The hydrazone (A below) dissolved, leaving a residue of azo-anilide, which was crystallised from alcohol and thrice from glacial acetic acid. 2-p-*Nitrobenzeneazo*cyclo*pentanone-2-carboxyanilide* (I; R = NHPh, R′ = $C_6H_4 \cdot NO_2$) *formed short lemon-yellow needles* (4 g.), *m. p.* 242°, sparingly soluble *in* organic solvents, insoluble in alkali (Found: C, 60·9, 61·1; H, 4·3, 4·1; N, 16·1. $C_{18}H_{16}O_3N_4$ *requires C,* 61·3; *H,* 4·5; *N,* 15·9%). *The same compound was prepared in good yield by* coupling the anilide with *p*-nitrobenzenediazonium sulphate in acetic acid. The alkaline extract (A) yielded on acidification *cyclo*pentane-1 : 2-*dione mono-p-nitrophenylhydrazone* (1·2 g.), *m. p.* 242° after crystallisation from alcohol, identical with material prepared from the keto-ester.

2-o-*Nitrobenzeneazo*cyclo*pentanone-2-carboxyanilide*, prepared in the same way as the *p*-nitro-compound, in 40% yield, formed yellow needles from acetic acid, turning orange on standing, m. p. 177° (Found: C, 60·8; H, 4·6%). The alkali-soluble by-product from this preparation was *cyclo*pentane-1 : 2-dione mono-*o*-nitrophenylhydrazone, m. p. 177°, not depressed by admixture with material prepared from the keto-ester (above), but depressed to 130—160° by admixture with the corresponding azo-anilide, m. p. 177°.

2 : 4-Dinitroaniline was diazotised as described above and coupled with 10 g. of *cyclo*pentanonecarboxyanilide, dissolved in 100 c.c. of acetic acid. The deposit of yellow crystals was collected after an hour and recrystallised from acetic acid. 2-(2′ : 4′-*Dinitrobenzeneazo*)cyclo*pentanone-2-carboxyanilide* formed yellow needles (14 g.), m. p. 206—207°, sparingly soluble in organic solvents, soluble in sodium hydroxide solution with a red colour (Found: C, 54·1; H, 4·0. $C_{18}H_{15}O_6N_5$ requires C, 54·4; H, 3·8%).

Bis*cyclo*pentanone-2-carboxybenzidide condensed readily with diazotised *o*- and *p*-nitroanilines and 2 : 4-dinitroaniline. The products were, however, extremely difficult to purify owing to their insolubility, and the procedure need not be detailed. *Bis*-2-o-*nitrobenzeneazo*-cyclo*pentanone-2-carboxybenzidide* formed vermilion needles from acetic acid, m. p. 265—268° (decomp.) (Found: C, 61·5; H, 4·5%). The corresponding p-*nitro*-compound was an orange powder, m. p. 245—250° (decomp.) (Found: C, 61·5; H, 4·6. $C_{36}H_{30}O_8N_8$ requires C, 61·7; H, 4·7%).

cyclo*Hexane Series.*

Unless otherwise stated, the methods used resembled those already described for the *cyclo*-pentane analogues.

Intermediates.—Sen and Basu (*J. Indian Chem. Soc.*, 1929, **6**, 313) described the preparation of *cyclo*hexanone-2-carboxyanilide from the ester, but did not analyse the product, and stated that it was insoluble in alkali. By the method described above for *cyclo*pentanecarboxyanilide, the anilide was obtained in 70% yield. It formed colourless plates from ether–light petroleum, m. p. 106—107° (Sen and Basu, 104—105°) (Found: C, 71·7; H, 6·8. Calc. for $C_{13}H_{15}O_2N$: C, 71·9; H, 6·9%). It was soluble in 1% aqueous sodium hydroxide, but the addition of less dilute alkali precipitated a sparingly soluble sodium compound. This accounts for the reported insolubility in alkali. The only by-product from the preparation was *s*-diphenylurea, m. p. and mixed m. p. 235—236° (compare Oppenheim and Drecht, *Ber.*, 1876, **9**, 1098; Knorr, *Annalen*, 1886, **236**, 69). When the keto-ester (16 g.) was kept with 9 g. of aniline over sulphuric acid in a vacuum desiccator for 4 days, it yielded the anil. This formed large prisms (11 g.) from light petroleum, m. p. 57—58 in agreement with Sen and Basu (*loc. cit.*), who did not analyse their product (Found: C, 73·5; H, 7·8. Calc.: C, 73·5; H, 7·8%).

*cyclo*Hexanone-2-carboxylic acid, m. p. 78—80° (decomp.), and 1-phenyl-3 : 4-*cyclo*hexano-5-pyrazolone, m. p. 164—165° (Found: C, 72·7; H, 6·6. Calc.: C, 72·9; H, 6·5%), were made by Dieckmann's methods (*Annalen*, **1901**, **317**, 98; 102).

Coupling.—(i) *Ester.* In agreement with Jackson and Manske (*loc. cit.*) diazotised aniline coupled with a freshly prepared alkaline solution of ethyl *cyclo*hexanone-2-carboxylate to give ***ethyl hydrogen α-ketopimelate phenylhydrazone***, m. p. 140—141°, in good yield (Found: C, 61·7; H, 6·9. $C_{15}H_{20}O_4N_2$ requires C, 61·6; H, 6·8%). On hydrolysis with alcoholic potash this yielded ***α-ketopimelic acid phenylhydrazone***, which formed light yellow needles from ethyl acetate–petroleum, m. p. 153—154° (decomp.) (Found: C, 59·4; H, 6·4. $C_{13}H_{16}O_4N_2$ requires C, 59·1; H, 6·1%). 2 G. of this compound were reduced by tin and hydrochloric acid to α-aminopimelic

acid, isolated through its copper salt. This reacted slowly with hydrogen sulphide, on account of its sparing solubility. The amino-acid formed prismatic needles from water, dissolved in its own water of crystallisation at 100°, and then became anhydrous, m. p. 203—204°. Yield, 0·8 g.

Ethyl hydrogen α-ketopimelate p-*nitrophenylhydrazone*, similarly prepared, formed yellow prismatic needles, from benzene, m. p. 150°; it gave orange solutions in dilute alkali and green solutions in concentrated alkali (Found: C, 53·7; H, 5·7. $C_{15}H_{19}O_6N_3$ requires C, 53·4; H, 5·6%). The corresponding *acid* formed yellow needles from acetone–petroleum, m. p. 174—175° (decomp.) (Found: C, 50·2; H, 4·9. $C_{13}H_{15}O_6N_3$ requires C, 50·5; H, 4·9%).

Ethyl *cyclo*hexanone-2-carboxylate was hydrolysed with alkali at 0° for 24 hours and then coupled with diazotised aniline. In agreement with Lions (*loc. cit.*) the product was *cyclo*hexane-1 : 2-dione monophenylhydrazone, m. p. 183—184°, from which the osazone, m. p. 153—154°, of Coffey (*Rec. trav. chim.*, 1923, **42**, 528) was prepared. The use of *p*-nitroaniline similarly led to the formation of cyclo*hexane*-1 : 2-*dione mono*-p-*nitrophenylhydrazone* (VII, R = $C_6H_4{\cdot}NO_2$) in good yield; it formed orange-yellow needles from amyl acetate, m. p. 245—246° (decomp.) (Found: C, 58·2; H, 5·2. $C_{12}H_{13}O_3N_3$ requires C, 58·3; H, 5·3%). 2 G. of this compound were heated for 30 minutes in a water-bath with 2 c.c. of phenylhydrazine in alcoholic acetic acid, and the product precipitated with mineral acid. Crystallisation from acetic acid gave remarkably different results according to the rate of cooling. Rapid cooling of a concentrated solution yielded small orange prisms; slow cooling of a more dilute solution yielded long indigo-blue needles. Both were cyclo*hexane*-1 : 2-*dione phenylhydrazone* p-*nitrophenylhydrazone*, and yielded an orange powder, m. p. 243—244 [Found: C, 64·5; H, 5·7 (orange); C, 64·2; H, 5·8 (indigo-blue). $C_{18}H_{19}O_2N_5$ requires C, 64·1; H, 5·6%]. Treatment of *cyclo*hexane-1 : 2-dione monophenylhydrazone with *p*-nitrophenylhydrazine in acetic acid yielded indigo-blue crystals of the same mixed osazone, m. p. and mixed m. p. 243—244°.

p-Nitrobenzenediazonium sulphate was prepared from *p*-nitroaniline (13·6 g.) and butyl nitrite (12 g.) in acetic acid by the procedure already described for the 2 : 4-dinitro-compound. A solution of the diazonium salt, well washed with ether, in 50 c.c. of acetic acid was treated successively with 15 c.c. of ethyl *cyclo*hexanone-2-carboxylate and 10 g. of powdered sodium acetate. After 4 hours the solid product was filtered off and repeatedly crystallised from dilute acetic acid. *Ethyl* 2-p-*nitrobenzeneazo*cyclo*hexanone*-2-*carboxylate* (V) formed yellow needles, m. p. 130—131°, very soluble in organic solvents, insoluble in water and sodium bicarbonate, soluble with decomposition in sodium carbonate and hydroxide solution. Yield, 6 g., crystallisation being wasteful (Found: C, 56·2; H, 5·5. $C_{15}H_{17}O_5N_3$ requires C, 56·4; H, 5·3%). 5 G. of the azo-ester were warmed with 200 c.c. of 1% sodium carbonate solution until carbon dioxide was no longer evolved. The acidic product was isolated by means of ether and purified through sodium bicarbonate. Ethyl hydrogen α-ketopimelate *p*-nitrophenylhydrazone, so obtained, formed yellow needles (2 g.) from benzene, m. p. 150° alone or mixed with the product obtained by coupling in alkali. Hydrolysis yielded the corresponding acid hydrazone, m. p. 173—174° (decomp.).

(ii) *Acid.* Pure, freshly prepared *cyclo*hexanone-2-carboxylic acid (10 g.) was dissolved in alcohol (20 c.c.) and ice-water (200 c.c.) and treated with diazotised aniline (6·5 g.). The addition of 5 g. of sodium acetate caused an immediate evolution of carbon dioxide and separation of a yellow precipitate. This was crystallised from alcohol and identified as *cyclo*hexane-1 : 2-dione monophenylhydrazone, m. p. and mixed m. p. 183—184°. Under similar conditions diazotised *p*-nitroaniline gave the mono-*p*-nitrophenylhydrazone of the dione, m. p. and mixed m. p. 245—246°.

A solution of 5 g. of the pure keto-acid in 50 c.c. of acetic acid was treated with the diazonium sulphate from 4·6 g. of *p*-nitroaniline dissolved in 50 c.c. of acetic acid. The addition of sodium acetate caused an immediate evolution of carbon dioxide and *cyclo*hexane-1 : 2-dione mono-*p*-nitrophenylhydrazone was again formed. An attempt to isolate the azo-acid by dilution, without the addition of sodium acetate, failed.

(iii) *Anilide.* A solution of the diazonium sulphate prepared from 13·6 g. of *p*-nitroaniline in acetic acid (60 c.c.) was added at 0° to one of 21·7 g. of *cyclo*hexanone-2-carboxyanilide in 100 c.c. of acetic acid. After the addition of sodium acetate (10 g.) the mixture was kept overnight and diluted with water, and the solid crystallised twice from acetic acid and twice from alcohol. 2-p-*Nitrobenzeneazo*cyclo*hexanone*-2-*carboxyanilide* formed rather brownish-yellow needles, m. p. 214°, insoluble in dilute alkali solution (Found: C, 62·0; H, 5·0. $C_{19}H_{18}O_4N_4$ requires C, 62·3; H, 4·9%).

(iv) *Pyrazolone.* To a solution of 1-phenyl-3 : 4-*cyclo*hexano-5-pyrazolone (21·4 g.) in acetic

acid (100 c.c.) were added an acetic acid solution of *p*-nitrobenzenediazonium sulphate (from 13·6 g. of *p*-nitroaniline) and sodium acetate (10 g.). After standing overnight, the mixture was poured into water, and the product washed and pressed on a porous tile. It gradually changed into a hard cake. All attempts at crystallisation failed, the crude azo-pyrazolone decomposing in hot solvents. Yield of crude material, 30 g., m. p. 85—95° (decomp.). 10 G. were refluxed with 50 c.c. of absolute ethyl alcohol for 2 hours, the solvent distilled through a column, and the most volatile fraction redistilled. Acetaldehyde was identified in the fraction of b. p. $<60°$ (3 c.c.) as the dimedone derivative, m. p. 137—139°. The residue was freed from alcohol and distilled in steam, nitrobenzene being identified in the distillate by the preparation of *m*-dinitrobenzene, m. p. 89—90°. The tarry residue was shaken with dilute hydrochloric acid, and after filtration, the liquid was made alkaline and freed from tar by extraction with benzene. The alkaline solution on cautious acidification with acetic acid yielded the original pyrazolone, m. p. and mixed m. p. 164—165°.

10 G. of the crude azo-pyrazolone were treated successively with 20 c.c. of acetic acid, 20 c.c. of hydrochloric acid, and 10 g. of dimethylaniline. After 16 hours at 50—60°, the original powder had completely disappeared, leaving a paste of red crystals with a metallic reflex. This was poured into water, collected, and crystallised several times from dilute hydrochloric acid. *p*-Nitrobenzeneazodimethylaniline hydrochloride separated in deep red crystals with a metallic lustre. Yield: 12 g. (crude), 5 g. (pure). The substance was identified by conversion into the free azo-base, m. p. and mixed m. p. 228—229°.

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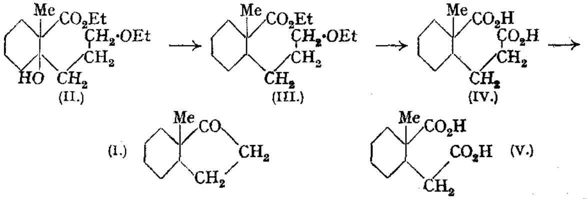
167. *The Synthesis of Dicyclic α-Ketones with an Angular Methyl Group.*

By G. A. R. KON, R. P. LINSTEAD, and C. SIMONS.

8-*Methyl*-1-*hydrindanone* (I) contains the essential structure of half the molecule of equilenin, œstrone, and other sex hormones. Its synthesis thus serves as a useful model for those of the natural compounds.

The work which we now describe is part of a general investigation, still in progress, of methods of synthesising α-ketones of this type. We have been led to publish an account of the synthesis of 8-methyl-1-hydrindanone and the corresponding decalone by the appearance of a paper by Chuang, Tien, and Ma (*Ber.*, 1936, **69**, 1494), which describes the preparation of the same compounds by a different method. Our methylhydrindanone, which we believe to be stereochemically homogeneous, differs in some respects from that of the Chinese workers.

The new synthetic method consists in the condensation of ethyl 2-methyl*cyclo*hexanone-2-carboxylate with the Grignard reagent prepared from γ-ethoxypropyl bromide, to the *hydroxy-ester* (II),* which by dehydration and reduction yields the saturated *ester* (III).



* Since this paper was written, Robinson and Walker (this vol., p. 61) have described a condensation essentially similar to the above, but did not carry the preparation beyond the first two steps.

This compound showed the expected resistance to hydrolysis and the corresponding ethoxy-acid could only be obtained by repeated treatment with alcoholic potash. The acid on oxidation with chromic acid yielded an acid containing 2-methyl*cyclo*hexane-2-carboxylic-1-β-propionic acid (IV); an indirect method, involving the conversion of the ethoxy-acid into the corresponding iodo-acid and subsequent oxidation, was less successful. The dibasic acid has not so far been isolated in a pure condition, but the crude acid gave, on heating with a little baryta, 8-methyl-1-hydrindanone (I), which could readily be purified by regeneration from the semicarbazone.

Chuang, Tien, and Ma (*loc. cit.*) describe this ketone as a liquid yielding a semicarbazone melting in the crude state at 205—210° and after purification at 213°. Our *semicarbazone* melted in the crude state at 220—222° and after exhaustive crystallisation at 224·5°; the initial material, therefore, was nearly homogeneous. The regenerated *ketone* was a solid, closely resembling camphor (with which it is isomeric) in odour and appearance and melting at 34°. Oxidation of the pure ketone with nitric acid led to 2-methyl*cyclo*hexane-2-carboxylic-1-acetic acid (V), m. p. 163°, identical with that synthesised by Linstead and Millidge (J., 1936, 478, following Chuang, Tien, and Huang, *Ber.*, 1935, **68**, 864). As Chuang, Tien, and Ma's ketone also yielded this acid on oxidation, it is clear that it must have contained a large amount of the same stereoisomeric form; the fact that it was liquid and gave a lower-melting semicarbazone is probably due to the presence of stereoisomeric impurity.

The *trans*-configuration had been provisionally assigned to the acid of m. p. 163° (Linstead and Millidge, *loc. cit.*), but further work by one of us (R. P. L.) and Mr. Walpole casts doubt on this, and for the moment we prefer to leave the question of the configuration of these substances open.

By an entirely similar method we have obtained 9-*methyl*-1-*decalone*, starting with ethyl methyl*cyclo*hexanonecarboxylate and δ-ethoxybutyl bromide. The *semicarbazone* of this compound had the same melting point as that described by Chuang, Tien, and Ma (*loc. cit.*); the ketone regenerated from it was a liquid but otherwise very similar to the ketone (I).

EXPERIMENTAL.

Ethyl 1-*Hydroxy*-2-*methyl*-1-(γ-*ethoxypropyl*)cyclo*hexane*-2-*carboxylate* (II).—60 G. of γ-ethoxypropyl bromide (Noyes, *Amer. Chem. J.*, 1897, **19**, 767), 30 c.c. of ether, and a crystal of iodine were added to 9 g. of magnesium. As the reaction proceeded, 300 c.c. of ether were gradually added; when no further action took place, the solution was decanted from unchanged metal and gradually dropped into an ice-cold ethereal solution of 48 g. of ethyl 2-methyl*cyclo*hexanone-2-carboxylate; a white solid was precipitated. The mixture was boiled under reflux for 2 hours, cooled, and decomposed with ice and dilute hydrochloric acid. The ethereal solution of the products was washed with sodium bicarbonate solution and water and dried over sodium sulphate, the ether distilled off, and the residue fractionated. The desired fraction (50 g.) boiled at 144°/4 mm. (Found: C, 66·0; H, 10·3. $C_{15}H_{28}O_4$ requires C, 66·1; H, 10·4%). A solid acid was not obtained on alkaline hydrolysis.

Ethyl 2-*Methyl*-1-(γ-*ethoxypropyl*)-$\Delta^{6(1)}$-cyclo*hexene*-2-*carboxylate*.—50 G. of the hydroxy-ester were boiled under reflux for 16 hours with 50 g. of oxalic acid and 50 c.c. of water. The acid was then neutralised with caustic soda, the ester extracted with ether, and the extract washed, dried over sodium sulphate, and evaporated, yielding the unsaturated *ester* (40 g.), b. p. 122°/2 mm. (Found: C, 70·4; H, 10·4. $C_{15}H_{26}O_3$ requires C, 70·8; H, 10·3%). The ester was unsaturated to bromine and to tetranitromethane and did not give a solid acid on hydrolysis.

Ethyl 2-*Methyl*-1-(γ-*ethoxypropyl*)cyclo*hexane*-2-*carboxylate* (III).—The unsaturated ester (35 g.) in 40 c.c. of acetic acid (distilled over chromic acid) was shaken with hydrogen and 0·75 g. of Adams's catalyst, 3100 c.c. of hydrogen being taken up. The solution was filtered from the catalyst, and the *ester* isolated by addition of water and extraction with ether, the extract being washed with alkali and water, dried, and evaporated; 33 g. of b. p. 123°/3 mm. were thus obtained and found to be saturated to tetranitromethane (Found: C, 70·8; H, 11·0. $C_{15}H_{28}O_3$ requires C, 70·3; H, 11·0%). The ester was not hydrolysed by boiling with dilute hydrochloric acid (2 : 1) for 6 hours, with 15% aqueous-alcoholic potassium hydroxide for 21 hours, or with a mixture of 3 parts of hydrochloric acid, 4 parts of acetic acid, and 1 part of water for 24

hours. Finally, 49 g. of the ester were boiled under reflux with 20 g. of potassium hydroxide in 70 c.c. of methyl alcohol for 5 hours, the solvent distilled off, and the unchanged ester extracted with ether and re-hydrolysed. After three such treatments 44 g. of crude acid together with 1·5 g. of neutral material were obtained; the acid did not solidify.

*2-Methyl*cyclo*hexane-2-carboxylic-1-β-propionic Acid* (IV).—(1) An ice-cold suspension of 7 g. of the ester (III) in 20 c.c. of hydriodic acid (saturated at 0°) was saturated with hydrogen iodide, kept for an hour, and then boiled under reflux until no more ethyl iodide was given off. The mixture was extracted with ether, and the iodo-acid (6 g.) recovered from the extract by shaking with alkali and re-acidification. It did not solidify; it was dissolved in 13 c.c. of acetic acid and treated with a solution of 6·5 g. of chromic acid in 6 c.c. of water and 14 c.c. of acetic acid. Much heat was evolved and iodine was liberated; the solution was then boiled for 40 minutes. The cold solution was diluted and extracted with ether, and the acid converted into the silver salt. This decomposed on boiling; the acid was recovered from it by means of nitric acid and isolated in the usual way, but the yield was poor (0·5 g.). The acid was a pasty solid with an equivalent of 134 (Calc. for the acid IV, 107).

(2) 8 G. of the ester (III) in 25 c.c. of acetic acid were treated with 17·5 g. of chromic acid in 60 c.c. of acetic acid. Much heat was evolved; the green solution was freed from acetic acid under reduced pressure and extracted with ether. The residue obtained after removal of the ether was converted into the potassium salt, and the solution filtered from chromium hydroxide and acidified. The acid obtained by extraction with ether had, after removal of traces of acetic acid, an equivalent of 211 and was therefore monobasic; it was presumably the half-ester of the required acid.

(3) The crude ethoxy-acid (44 g.) in 90 c.c. of acetic acid was gradually treated with 65 g. of chromic acid in 130 c.c. of acetic acid and 10 c.c. of water, causing the evolution of much heat. The reaction was completed by warming on the steam-bath for 75 minutes. After addition of 800 c.c. of water the solution was extracted eight times with ether, and the extract evaporated; the residue was distilled under reduced pressure to remove acetic acid and then purified as described under (2) above; 15 g. of crude acid with an equivalent of 130 were obtained. It did not solidify in an evacuated desiccator after a month and a pure silver salt could not be obtained; an attempt to purify it through the ester was also unsuccessful.

8-Methyl-1-hydrindanone (I).—1·2 G. of crystalline baryta and 15 g. of the crude dibasic acid, freed from the last traces of acetic acid by warming in a high vacuum, were slowly distilled from a Claisen flask kept at 275—320°. The distillate was taken up in ether, washed with dilute caustic soda solution, then water, dried, and distilled, yielding 4 g., b. p. 84°/5 mm., together with 1 g. of a higher fraction. The latter gave but little semicarbazone, whereas the main fraction gave a copious precipitate of a *semicarbazone*, m. p. 224·5° after three crystallisations from methyl alcohol (Found: C, 63·3; H, 9·2. $C_{11}H_{19}ON_3$ requires C, 63·1; H, 9·2%). The *ketone* regenerated from it by means of oxalic acid distilled at 84°/5 mm. as a colourless liquid, which rapidly solidified to a camphor-like mass, m. p. 33—34° (Found: C, 78·1; H, 10·8. $C_{10}H_{16}O$ requires C, 78·9; H, 10·6%).

*2-Methyl*cyclo*hexane-1-carboxylic-2-acetic Acid* (V).—1·2 G. of the ketone were warmed under reflux for 45 minutes with 6 c.c. of concentrated nitric acid, then for 2 hours longer with the addition of 5 c.c. of water, an all-glass apparatus being used. The solid acid obtained on cooling was recrystallised from very dilute acetic acid, forming a microcrystalline powder, m. p. 162—163°, mixed m. p. with a genuine specimen of the acid 163° (Found: C, 60·2; H, 8·4. Calc. for $C_{10}H_{16}O_4$: C, 60·0; H, 8·1%).

δ-Ethoxybutyl Bromide.—The corresponding alcohol was obtained from γ-ethoxypropyl bromide by the method of Palomaa and Jansson (*Ber.*, 1931, **64**, 1606), who used the chloride. The *bromide*, prepared from it by the method used by Noyes (*loc. cit.*) for the preparation of the lower homologue, boiled at 169°, the yield being 35 g. from 47 g. of the alcohol (Found: Br, 43·6. $C_6H_{11}OBr$ requires Br, 44·2%). This preparation and the analysis were first carried out in these laboratories by Dr. P. A. Winsor.

*Ethyl 1-Hydroxy-2-methyl-1-(δ-ethoxybutyl)*cyclo*hexane-2-carboxylate.*—A Grignard reagent, prepared from 21 g. of δ-ethoxybutyl bromide, was treated with ethyl 2-methyl*cyclo*hexanone-2-carboxylate exactly as described on p. 815; no precipitate was produced. The product gave 14 g. of the *ester*, b. p. 165°/0·5 mm. (Found: C, 66·9; H, 10·5. $C_{16}H_{30}O_4$ requires C, 67·1; H, 10·6%).

*Ethyl 2-Methyl-1-(δ-ethoxybutyl)-$\Delta^{6(7)}$-*cyclo*hexene-2-carboxylate.*—The hydroxy-ester (24 g.) was dehydrated in the course of 19 hours as described on p. 815 and gave 20 g. of the unsaturated *ester*, b. p. 135°/0·4 mm. (Found: C, 71·2; H, 10·6. $C_{16}H_{28}O_3$ requires C, 71·6; H, 10·5%).

Ethyl 2-Methyl-1-(δ-ethoxybutyl)cyclohexane-2-carboxylate.—The reduction of the unsaturated ester (19 g.) was carried out as described on p. 815; some 1800 c.c. of hydrogen were taken up and 17 g. of the saturated *ester* were obtained, b. p. 149°/0·8 mm. (Found: C, 70·7; H, 11·3. $C_{16}H_{30}O_3$ requires C, 71·1; H, 11·2%). The ester was hydrolysed by the method given on p. 816; the acid did not solidify and was used for the next step without purification.

9-Methyl-1-decalone.—The crude ethoxy-acid (13 g.) in 26 c.c. of acetic acid was treated with 18 g. of chromic acid in 36 c.c. of acetic acid and 4 c.c. of water in quantities of 2—3 c.c. at a time, and the mixture finally warmed on the steam-bath for an hour. The acetic acid was distilled off under reduced pressure, and the residue dissolved in 10% sodium hydroxide solution. The solution was boiled and filtered, and the precipitate washed with water. The filtrate was concentrated to 200 c.c., acidified, and extracted with ether. The extract was evaporated, finally in a high vacuum, and the residue of crude dibasic acid distilled with the addition of 0·4 g. of baryta at 310° (bath temperature). The distillate was taken up in ether and washed with caustic soda solution, the solvent removed, and the residue treated with semicarbazide acetate. The *semicarbazone*, which formed with some difficulty, had m. p. 223° after several crystallisations (yield, 0·8 g.) (Found: C, 64·7; H, 9·5. $C_{12}H_{21}ON_3$ requires C, 64·5; H, 9·5%). The ketone regenerated from it was a liquid which did not solidify in a freezing mixture.

Alternative Preparation of 9-Methyl-1-decalone.—21 G. of the crude iodo-acid prepared as described on p. 816 were treated with an ice-cold mixture of 10 c.c. of absolute alcohol and 1·4 c.c. of sulphuric acid. After being left in a freezing mixture for 3—4 hours and at room temperature for 2 days, the oily mass deposited crystals. It was taken up in ether, and the extract washed with sodium carbonate solution and water, dried, and evaporated; 13 g. of solid *ethyl 2-methyl-1-(γ-iodopropyl)cyclohexane-2-carboxylate* were obtained, which formed plates from dilute alcohol, m. p. 94° (Found: I, 38·2. $C_{13}H_{23}O_2I$ requires I, 37·5%); 6 g. of the acid were recovered from the alkaline washings and were re-esterified.

16 G. of the iodo-ester were heated with 3·5 g. of potassium cyanide in 3·5 c.c. of alcohol and 1 c.c. of water for 24 hours. Without isolation of the nitrile formed, 15 g. of potassium hydroxide in 45 c.c. of 50% alcohol were added, and the mixture boiled for 7 hours. The liquid was then acidified and warmed for an hour to decompose the alkali cyanide, and the oil extracted with ether and re-hydrolysed with 65 c.c. of 15% aqueous potassium hydroxide to ensure that no acid ester remained (4 hours). On working up, 5·5 g. of a light brown acidic gum were obtained; this did not crystallise and on heating with a little baryta gave a poor yield of the dicyclic ketone, identified by the semicarbazone (m. p. 222°, mixed m. p. 223°).

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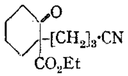
168. *The Synthesis of Polyterpenoid Compounds. Part III.*

By J. W. COOK and C. A. LAWRENCE.

IN Part II (J., 1935, 1637) we gave the first example of a new method of synthesis of polycyclic hydroaromatic ketones by intramolecular condensation of an unsaturated acid chloride of suitable structure. In the further development of our work we have been to some extent anticipated by Chuang, Tien, and Ma (*Ber.*, 1936, **69**, 1494), who adapted our method to the synthesis of hydronaphthalenes containing an "angular" methyl group, and of the hydrindane (perhydroindene) system. We were ourselves occupied with both these projects when the paper of the Chinese authors appeared, and had in fact completed the former scheme, using a simpler route than that taken by Chuang and his collaborators. We now record our own experiments, except in so far as they are duplicated by those of Chuang *et al.* The extension of the synthetic methods to more complex ring systems is in progress.

For the synthesis of γ-Δ^1-*cyclo*hexenylbutyric acid, required for cyclisation to $\Delta^{9:10}$-1-octalone (Part II), we had introduced the butyric acid side chain in two stages, a procedure followed by Chuang. This can, however, be effected in one stage, condensation of ethyl potassio*cyclo*hexanone-2-carboxylate with γ-iodobutyronitrile leading to *ethyl 2-γ-cyanopropyl*cyclo*hexanone-2-carboxylate* (I), which was hydrolysed by dilute alkali to γ-2-keto-

*cyclo*hexylbutyric acid (II), a compound formerly obtained by Hückel and Naab (*Annalen*, **1933**, **502**, 146) by oxidation of $\Delta^{1:9}$-octahydronaphthalene. A by-product of the hydrolysis was *octane-αδθ-tricarboxylic acid.* The *ethyl* ester of the keto-acid (II) reacted with methylmagnesium iodide to give a product which, after hydrolysis and dehydration, gave γ-(2-methyl-Δ^1-*cyclo*hexenyl)butyric acid (III), which was synthesised by Chuang, Tien, and Ma (*loc. cit.*) by another method. Cyclisation of (III) led to 9-methyl-$\Delta^{4:10 \text{ (or } 5:10)}$-1-octalone, which was hydrogenated to 9-methyl-1-decalone (IV), the properties of which agreed with those cited by Chuang, Tien, and Ma.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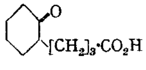
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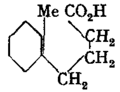
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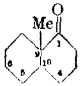
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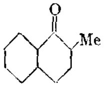
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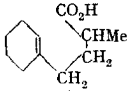

(VI.)

A ketone of type (IV), with a methoxyl group at position 6, would furnish a suitable starting point for the synthesis of a sterol type of molecule. Synthesis of (IV) from *cyclo*hexanone is laborious, and it seemed possible that the angle methyl group might be introduced directly into the molecule of α-decalone. However, treatment of the sodio-derivative of *trans*-1-decalone with methyl iodide led to a complex mixture, from which was isolated only a small amount of the 9-methyl derivative (IV). The principal product was 2-*methyl*-1-*decalone* (V),* and a third *ketone*, probably stereoisomeric with (IV) or (V), was also isolated. The structure of (V) was shown by its synthesis from β-Δ^1-*cyclo*hexenylethyl bromide and ethyl methylmalonate, with subsequent hydrolysis and decarboxylation of the product, and then cyclisation of the resulting γ-Δ^1-cyclo*hexenyl-α-methylbutyric acid* (VI), followed by hydrogenation of the 2-*methyl*-$\Delta^{9:10}$-1-*octalone*.

In an attempt to extend these reactions to synthesis in the sesquiterpene field we have studied the condensation of β-(4-methyl-Δ^1-*cyclo*hexenyl)propyl bromide with ethyl potassiomalonate, and of ethyl γ-bromovalerate with ethyl potassio-5-methyl*cyclo*hexanone-2-carboxylate. The disappointingly small yields of the products (VII and VIII, respectively) have made it impracticable to attain our objective, although (VII) was transformed through the usual stages into 1 : 6-*dimethyl*-$\Delta^{9:10}$-4-*octalone* (IX), which, if available in sufficient quantity, should be readily convertible into a hydrocarbon (X) differing structurally from α- or β-cadinene only in the disposition of one double bond.

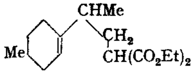
Nenitzescu and Ciorănescu (*Ber.*, 1936, **69**, 1820) have shown that the reaction between acid chlorides and *cyclo*olefins leads to *saturated* ketones if carried out in the presence of aluminium chloride and *cyclo*hexane, the latter acting as a hydrogen donor. This type of reduction did not occur when γ-Δ^1-*cyclo*hexenylbutyryl chloride was treated under similar conditions with aluminium chloride and *cyclo*hexane, the sole ketonic product being $\Delta^{9:10}$-1-octalone. This experience tallies with that of Robinson and Walker (this vol., p. **61**), who likewise observed no reduction in an analogous case.

We are also occupied with possible applications of the Diels–Alder diene reaction to the synthesis of polycyclic hydroaromatic compounds. We merely report now that addition

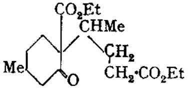
* *Note on Configuration.*—It is probable that our 2-methyl-1-decalone is one of the two possible racemic *trans*-forms. This is supported by the preparation of the compound both by methylation of *trans*-1-decalone and by hydrogenation of 2-methyl-$\Delta^{9:10}$-1-octalone. The hydrogenation of $\Delta^{9:10}$-1-octalone is known to give largely the *trans*-decalone (Hückel and Blohm, *Annalen*, **1933**, **502**, 136). The optical exaltation of 2-methyl-1-decalone (+0·25) also accords with a *trans*-fusion of the rings.

In the case of our 9-methyl-1-decalone the synthetic methods warrant no conclusion concerning the configuration, but the slight optical depression (−0·06) suggests the *cis*-configuration.

products could not be obtained from Δ^1-tetrahydrobenzoic acid and butadiene or 2 : 3-dimethylbutadiene, or from Δ^1-tetrahydrobenzaldehyde and 2 : 3-dimethylbutadiene.



(VII.)



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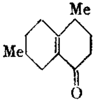
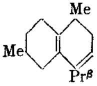
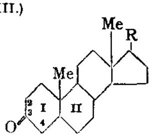


(IX.)

(X.)





(XI.)

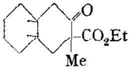
Subsequently, Fieser and Holmes (*J. Amer. Chem. Soc.*, 1936, **58**, 2319) reported the slow formation of adducts from ethyl Δ^1-dihydronaphthoate and butadiene or 2 : 3-dimethylbutadiene. We therefore re-examined one of our examples, and heated ethyl Δ^1-tetrahydrobenzoate with 2 : 3-dimethylbutadiene for 196 hours at 105—110°, but no addition occurred.

Sterol ketones (XI) are brominated at position 2 and oxidised with fission of the 2 : 3-bond when there is a *trans*-fusion of rings I and II, but brominated at position 4 and oxidised with fission mainly of the 3 : 4-bond in the corresponding *cis* series (for references, see *Ann. Reports*, 1936, **33**, 344). If similar differences of reactivity could be shown to hold for simpler dicyclic derivatives of *cis*- and *trans*-2-decalones, then compounds of the *cis*-series, but not of the *trans*-series, could be used in the synthesis of perhydrophenanthrene derivatives by extension of the methods described above (see also Robinson, J., 1936, 1088; du Feu, McQuillin, and Robinson, this vol., p. 54). There can be little doubt that the differences observed in the sterol ketones are due to the different positions favoured by the enolic double bonds in the two stereoisomeric series, in which case different positions should likewise be taken up by the double bonds arising from the dehydration of corresponding series of 3-hydroxy-compounds. There appears to be little available evidence on this point. However, in the case of the β-decalols it has been shown that dehydration of *trans*-2-decalol (m. p. 75°) gives 90% of *trans*-Δ^2-octalin (Hückel and Naab, *Annalen*, 1933, **502**, 151; compare Leroux, *Ann. Chim.*, 1910, **21**, 471), whereas the dehydration of *cis*-2-decalol (m. p. 105°) gives both the Δ^1- and the Δ^2-octalin, the proportion depending to some extent on the dehydrating agent used, but never being predominantly in favour of the Δ^1-compound (Hückel, *Ber.*, 1925, **58**, 1451; Hückel and Friedrich, *Annalen*, 1927, **451**, 147). Also, the formation of the ring system of 1 : 2-benzanthracene to the exclusion of that of 3 : 4-benzphenanthrene by cyclisation of the phenylethyloctalin resulting from the dehydration of 2-β-phenylethyl-*trans*-2-decalol (Cook and Hewett, J., 1934, 375) indicates that the octalin is essentially the Δ^2-compound. Hückel (*Annalen*, 1925, **441**, 17) and Hückel and Friedrich (*loc. cit.*) have also studied the oxidation of the above-mentioned *cis*- and *trans*-2-decalols to the corresponding dicarboxylic acids; presumably the ketones are intermediate products. The results show no clear-cut differences between the two stereoisomeric series, such as is encountered with the sterol derivatives.

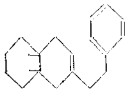
In substitution reactions *trans*-2-decalone is attacked mainly at position 3, the 3-chloro-derivative having been described by Lehmann and Krätschell (*Ber.*, 1934, **67**, 1867), and the ethyl 3-glyoxylate by Hückel and Goth (*Ber.*, 1925, **58**, 449). By monochlorination of *cis*-2-decalone we have obtained 3-*chloro*-cis-2-*decalone* (XII), the orientation of which was shown by its hydrolysis to 3-*hydroxy*-cis-2-*decalone*, followed by oxidation to *cis*-*cyclo*hexane-1 : 2-diacetic acid. *cis*-2-Decalone condensed with ethyl oxalate to give ethyl *cis*-2-ketodecalyl-3-glyoxylate, which was thermally degraded to *ethyl* cis-2-*decalone*-3-

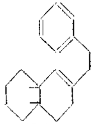
carboxylate. In order to determine the orientation of this keto-ester its sodio-derivative was methylated with methyl iodide, and the resulting *ethyl* 3-*methyl*-cis-2-*decalone*-3-*carboxylate* (XIII) was dehydrogenated with selenium to 3-methyl-2-naphthol, the properties of which agreed with those given by Veselý and Štursa (*Coll. Czech. Chem. Comm.*, **1934**, **6**, 137). The same naphthol was similarly obtained from ethyl *trans*-2-decalone-3-carboxylate.

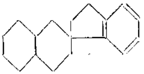
(XII.)

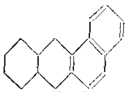
 (XIII.)

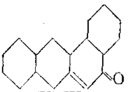
We have also studied the cyclisation with aluminium chloride at 0° of the *phenylethyloctalin* which arises from the dehydration of 2-β-*phenylethyl*-cis-2-*decalol*. The unsaturated hydrocarbon, which could contain (XIV) and (XV), was cyclised to a mixture of hydrocarbons, from which was isolated the same dodecahydro-1 : 2-benzanthracene, m. p. 72°, previously prepared from *trans*-2-decalone (Cook and Hewett, *loc. cit.*).

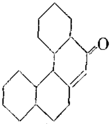

(XIV.)


(XV.)


(XVI.)


(XVII.)


(XVIII.)


(XIX.)

Evidently change in configuration occurs during cyclisation with aluminium chloride, analogous to the conversion of *cis*- into *trans*-decalin (Zelinsky and Turowa-Pollak, *Ber.*, 1932, **65**, 1299). Dehydrogenation of the mixture of saturated hydrocarbons gave 1 : 2-benzanthracene, 5 : 6 : 7 : 8-tetrahydro-1 : 2-benzanthracene, *octahydro*-1 : 2-*benzanthracene* (XVII), and a small amount of chrysene. There was no evidence of the presence of 3 : 4-benzphenanthrene (from XV). The chrysene probably arises from (XVI) by rearrangement during dehydrogenation (compare Cook and Hewett, J., 1934, 365). Hence, the cyclisation products are mainly stereoisomeric dodecahydrobenzanthracenes, so that the phenylethyloctalin is mainly the Δ^2-compound (XIV), as in the *trans*-series. We cannot exclude the possibility that the *cis*-octalin (XIV) is *completely* converted into its *trans*-isomeride *prior to* ring closure, in which event this argument is not valid.

Additional evidence, not open to such objection, that position 3 is the main position of reactivity of *cis*-2-decalone was secured by utilising the condensation method developed by Rapson and Robinson (J., 1935, 1285; 1936, 757, 759, 763). The sodio-compounds of both *cis*- and *trans*-2-decalones were condensed with acetyl-Δ^1-*cyclo*hexene to give mixtures of ketones, of which the main constituents (in fact the only constituents which could be isolated) were the two stereoisomeric 3-*keto*-Δ^4-*hexadecahydro*-1 : 2-*benzanthracenes* (XVIII), in which the ring systems were established by dehydrogenation to 1 : 2-benzanthracene. In the case of the condensation with *cis*-2-decalone the distilled mixture of ketones was reduced by Clemmensen's method, and the hydrocarbon mixture dehydrogenated with platinum-black. In addition to 1 : 2-benzanthracene, a small amount of 3 : 4-benzphenanthrene was isolated, indicating the presence of the ketone (XIX) in the original mixture.

These results provide ample demonstration that the striking differences in the position of substitution shown by the stereoisomeric sterol ketones (XI) do not hold in the case of the

simpler 2-decalones, both *cis*- and *trans*-compounds being attacked mainly at position 3. Evidently the stability of the alternative Δ^1- and Δ^2-octalin systems present in the enolic forms of the ketones is influenced by the locking of this portion of the sterol molecule with the remainder of the ring system. Incidentally, the method envisaged by Robinson (J., 1936, 1088) for the synthesis of testosterone would appear to be precluded by these results.

EXPERIMENTAL.

Synthesis of α-Decalone Derivatives.

*Ethyl 2-γ-Cyanopropyl*cyclo*hexanone-2-carboxylate* (I).—γ-Chlorobutyronitrile (50 g.) ("Organic Syntheses," Collective Vol. I, p. 150) was converted into the corresponding iodo-compound by refluxing for 12 hours with sodium iodide (100 g.) in ethyl alcohol (400 c.c.). The filtered solution was concentrated under reduced pressure, and the residue extracted with ether, washed free from iodine with sodium thiosulphate solution, dried, and distilled. The γ-iodobutyronitrile (85% yield) had b. p. 109°/10 mm. (Case, *J. Amer. Chem. Soc.*, 1933, **55**, 2929, gives 113—116°/7 mm.). This γ-iodobutyronitrile (79·4 g.) was added to a suspension of the sodio-compound prepared from ethyl *cyclo*hexanone-2-carboxylate (70 g.) and sodium powder (9 g.) in benzene (300 c.c.), and the mixture heated on the water-bath for 50 hours. Water was then added, and the benzene layer washed, dried (calcium chloride), and distilled. *Ethyl 2-γ-cyanopropyl*cyclo*hexanone-2-carboxylate* (76·3 g.) formed a colourless viscous liquid, b. p. 163—165°/0·7 mm. (Found: C, 65·5; H, 8·8. $C_{13}H_{19}O_3N$ requires C, 65·8; H, 8·1%). The semicarbazone formed colourless hexagonal plates (from methyl alcohol), m. p. 176—177°.

γ-2-*Keto*cyclo*hexylbutyric Acid* (II).—The foregoing ester (70 g.) was heated for 4 hours on the water-bath with aqueous potassium hydroxide (53 g. in 1400 c.c.). Unhydrolysed material was extracted with ether, and re-treated with potassium hydroxide (6 g. in 160 c.c.). The combined alkaline liquors were acidified, saturated with sodium chloride, and extracted four times with ether. The washed and dried extract gave, on distillation, crude γ-2-keto*cyclo*hexylbutyric acid (33·4 g. = 62%), b. p. 168°/0·8 mm., and a brownish gum, b. p. 280—290°/0·8 mm. The latter fraction was evidently *octane-αδθ-tricarboxylic acid* (Found: C, 54·1; H, 7·5; equiv., 85·4. $C_{11}H_{18}O_6$ requires C, 53·6; H, 7·4%; equiv., 82·0). The *ethyl* ester, formed by refluxing with alcohol and sulphuric acid, was a colourless liquid, b. p. 162—163°/1 mm. (Found: C, 62·4; H, 9·2. $C_{17}H_{30}O_6$ requires C, 61·8; H, 9·2%). An analogous example of fission of the *cyclo*hexanone ring has been given by Haworth and Mavin (J., 1933, 1015), who obtained the corresponding heptanetricarboxylic acid as a by-product in the preparation of β-2-keto*cyclo*hexylpropionic acid.

The distilled keto-acid (II) crystallised on cooling and, after crystallisation from ether-light petroleum, had m. p. 58°. Its semicarbazone had m. p. 185—187°, and its oxime had m. p. 102—104°. The acid obtained by hydrolysis of the semicarbazone had m. p. 60—61°. Hückel and Naab (*loc. cit.*) give m. p. 60—61°, 189°, and 101—103° for this acid and its semicarbazone and oxime, respectively. The p-*phenylphenacyl* ester of γ-2-keto*cyclo*hexylbutyric acid formed colourless irregular plates (from alcohol), m. p. 78—79° (Found: C, 75·9; H, 7·0. $C_{24}H_{26}O_4$ requires C, 76·15; H, 6·9%). The *ethyl* ester (34 g.), prepared from the crude acid (34·7 g.) and sulphuric acid (3 c.c.) in alcohol (140 c.c.), formed a colourless liquid, b. p. 136°/0·4 mm. (Found: C, 67·7; H, 9·5. $C_{12}H_{20}O_3$ requires C, 67·9; H, 9·5%); its semicarbazone had m. p. 103—104°.

γ-(2-*Methyl*-Δ^1-cyclo*hexenyl*)*butyric Acid* (III).—A Grignard solution prepared from methyl iodide (17 g.), magnesium turnings (3·1 g.), and anhydrous ether (100 c.c.) was added dropwise, with stirring, to an ice-cold solution of ethyl γ-2-keto*cyclo*hexylbutyrate (24·5 g.) in ether (60 c.c.). After being kept at 0° for 2 hours, the mixture was decomposed with ice and ammonium chloride. The residue remaining after removal of the ether from the washed ethereal solution was hydrolysed by heating for 7 hours at 100° with potassium hydroxide (20 g.) in water (200 c.c.), with frequent shaking. After being extracted with ether, the alkaline solution was acidified, saturated with sodium chloride, and extracted four times with ether. The extract was dried (sodium sulphate), the ether removed, and the residue heated at 170—180° for 2 hours with potassium hydrogen sulphate (35 g.) in order to dehydrate the hydroxy-acid. The product was extracted and distilled at 0·4 mm. The higher fraction (5·1 g.), b. p. 150—152°, solidified on cooling and was mainly unchanged keto-acid. The lower fraction (12 g.), b. p. 134—142°, was essentially the desired γ-(2-methyl-Δ^1-*cyclo*hexenyl)butyric acid (III), and after redistillation had b. p. 123°/0·3 mm. (Found: C, 71·4; H, 9·7. Calc. for $C_{11}H_{18}O_2$: C, 72·5; H, 9·9%).

Its p-*phenylphenacyl* ester formed thin colourless plates, m. p. 83—84° (from alcohol) (Found : C, 79·5; H, 7·3. $C_{25}H_{28}O_3$ requires C, 79·8; H, 7·7%).

9-Methyl-$\Delta^{4:10 \text{ (or } 5:10)}$*-1-octalone and 9-Methyl-1-decalone.*—Cyclisation of the unsaturated acid (III) by the action of stannic chloride on its chloride was carried out as described for the lower homologue (J., 1935, 1638; see also Chuang, Tien, and Ma, *loc. cit.*). The semicarbazone of the 9-methyloctalone had m. p. 222—223° (decomp.) (Found: N, 19·2. Calc.: N, 19·0%); Chuang *et al.* give m. p. 226—227°. The 2 : 4-*dinitrophenylhydrazone* formed red plates (from alcohol or aqueous dioxan), m. p. 133° (Found: N, 16·2. $C_{17}H_{20}O_4N_4$ requires N, 16·3%). 9-Methyl-1-decalone (IV) was obtained by hydrogenation of the unsaturated ketone in alcoholic solution with palladium-black. After purification through its semicarbazone, m. p. 224—225° (Chuang *et al.* give 225—226°), the saturated ketone (IV) had b. p. 118°/20 mm., $n_D^{18\cdot8°}$ 1·4903, $d_4^{18\cdot8°}$ 0·9953; whence $[R_L]_D$ = 48·56 (calc., 48·61). The *oxime* formed thin lozenge-shaped plates (from aqueous methyl alcohol), m. p. 108·5—111° (Found: N, 7·85. $C_{11}H_{19}ON$ requires N, 7·7%), and the 2 : 4-*dinitrophenylhydrazone* formed orange tabular crystals (from alcohol containing a little dioxan), m. p. 159—160° (decomp.) (Found: N, 15·9. $C_{17}H_{22}O_4N_4$ requires N, 16·2%).

β-Δ^1-cyclo*Hexenylethylmethylmalonic Acid.*—The yield of β-Δ^1-*cyclo*hexenylethyl alcohol obtained by Bouveault reduction of ethyl Δ^1-*cyclo*hexenylacetate (Cook and Dansi, J., 1935, 500) was increased from 55% to 72% by the use of anhydrous alcohol, dried with magnesium methoxide. β-Δ^1-*cyclo*Hexenylethyl bromide (61·4 g.) was heated on the water-bath for 130 hours with the potassio-compound prepared from ethyl methylmalonate (60 g.) and potassium (13 g.) in pure benzene (350 c.c.). *Ethyl* β-Δ^1-cyclo*hexenylethylmethylmalonate* (53 g.), isolated in the usual manner, formed a colourless liquid, b. p. 134—137°/0·5 mm. (Found: C, 67·4; H, 9·5. $C_{16}H_{26}O_4$ requires C, 68·05; H, 9·3%). β-Δ^1-cyclo*Hexenylethylmethylmalonic acid*, formed by hydrolysis of the ester with alcoholic potash, separated from ligroin–benzene as a colourless crystalline powder, m. p. 141·5—142·5° (Found: C, 63·7; H, 8·4. $C_{12}H_{16}O_4$ requires C, 63·7; H, 8·0%).

γ-Δ^1-cyclo*Hexenyl-α-methylbutyric acid* (VI) was obtained in almost quantitative yield by heating the foregoing malonic acid at 180—190° for 20 minutes, and formed a colourless liquid, b. p. 140—145°/0·8 mm. (Found: C, 72·0; H, 10·6; equiv., 199·4, 203·4. $C_{11}H_{18}O_2$ requires C, 72·5; H, 9·9%; equiv., 182·1). The p-*phenylphenacyl* ester crystallised from alcohol in thin colourless plates, m. p. 88—90·5° (Found: C, 79·5; H, 7·7. $C_{25}H_{28}O_3$ requires C, 79·75; H, 7·6%).

2-Methyl-$\Delta^{9:10}$*-1-octalone.*—The unsaturated acid (VI) (12·1 g.) was converted into its chloride by the standard procedure (see Part II), by means of 50 c.c. of ether, 5·3 g. of pyridine, and 8·0 g. of thionyl chloride, and the acid chloride was cyclised to the octalone, which was obtained in 43% yield, 2·6 g. of acid being recovered (17 g. of stannic chloride, 20 c.c. of carbon disulphide, and 15 g. of dimethylaniline were employed). *2-Methyl-*$\Delta^{9:10}$*-1-octalone*, obtained analytically pure by hydrolysis of its semicarbazone with 2*N*-sulphuric acid at 100°, formed a colourless mobile liquid, b. p. 129°/13 mm., $n_D^{11\cdot2°}$ 1·5210, $d_4^{11\cdot2°}$ 1·022; whence $[R_L]_D$ = 48·90 (calc., 48·14) (Found: C, 80·6; H, 10·0. $C_{11}H_{16}O$ requires C, 80·4; H, 9·8%). The *semicarbazone* formed small colourless plates (from alcohol), m. p. 212° (decomp.) (Found: N, 18·9. $C_{12}H_{19}ON_3$ requires N, 19·0%); the *oxime* formed small colourless needles (from methyl alcohol), m. p. 160—161° (Found: N, 7·6. $C_{11}H_{17}ON$ requires N, 7·8%); and the 2 : 4-*dinitrophenylhydrazone* formed small, thick, red plates (from dioxan), m. p. 219—220° (decomp.) (Found: N, 16·2. $C_{17}H_{20}O_4N_4$ requires N, 16·3%).

2-Methyl-1-decalone (V).—The unsaturated ketone (2·5 g.) was hydrogenated in alcoholic solution (25 c.c.) with palladium-black (0·2 g.). The theoretical volume of hydrogen was absorbed in 2 hours. The *semicarbazone* of the saturated ketone (V) was recrystallised from alcohol until it had a constant m. p., 216—217·5° (decomp.) (Found: N, 19·55. $C_{12}H_{21}ON_3$ requires N, 18·8%). *2-Methyl-1-decalone* (V), obtained by hydrolysis of the semicarbazone, formed a colourless liquid, b. p. 109°/11 mm., which gave an unsatisfactory value for carbon (see, however, p. 824) (Found: C, 78·7; H, 10·8. $C_{11}H_{18}O$ requires C, 79·5; H, 10·9%). Its *oxime* formed long colourless needles (from aqueous methyl alcohol), m. p. 152—153·5° (Found: N, 8·05. $C_{11}H_{19}ON$ requires N, 7·7%), and its 2 : 4-*dinitrophenylhydrazone* formed orange tabular crystals (from aqueous dioxan), m. p. 223—224·5° (Found: N, 16·45. $C_{17}H_{22}O_4N_4$ requires N, 16·2%).

γ-(*4-Methyl-*Δ^1-cyclo*hexenyl*)*valeric Acid.*—By the use of alcohol dried with magnesium methoxide for the Bouveault reduction of ethyl α-(4-methyl-Δ^1-*cyclo*hexenyl)propionate (Cook and Dansi, *loc. cit.*) the yield of β-(4-methyl-Δ^1-*cyclo*hexenyl)propyl alcohol was raised to 80%. Condensation of β-(4-methyl-Δ^1-*cyclo*hexenyl)propyl bromide (55·9 g.) with the potassio-com-

pound from ethyl malonate (55 g.) and potassium (12 g.) in benzene (350 c.c.) (130 hours at 100°) gave only an 8·3% yield of ethyl β-(4-methyl-Δ^1-*cyclo*hexenyl)propylmalonate (VII), b. p. 138°/0·4 mm. Hydrolysis with alcoholic potash yielded an oily acid, which did not crystallise after 14 days in the ice-chest. It was therefore decarboxylated by heating at 180—190° for 20 minutes. The resulting *γ-(4-methyl-Δ^1-*cyclo*hexenyl)valeric acid* formed a colourless liquid, b. p. 112—114°/0·4 mm. (Found : C, 72·6; H, 10·45. $C_{12}H_{20}O_2$ requires C, 73·4; H, 10·3%).

1 : 6-*Dimethyl-$\Delta^{9:10}$-4-octalone* (IX).—Cyclisation of γ-(4-methyl-Δ^1-*cyclo*hexenyl)valeric acid (2·8 g.) in the usual manner gave the crude *ketone* (IX) (1 g.), b. p. 141°/13 mm., which was not obtained analytically pure (Found : C, 78·8; H, 10·0. $C_{12}H_{18}O$ requires C, 80·9; H, 10·2%). The *oxime* formed a colourless microcrystalline powder (from aqueous methyl alcohol), m. p. 98—102° (Found : N, 7·4. $C_{12}H_{19}ON$ requires N, 7·25%); the *semicarbazone* formed small, colourless, irregular crystals (from aqueous dioxan), m. p. 163—165·5° (clear at 169°) (Found : C, 65·7; H, 8·9; N, 17·7. $C_{13}H_{21}ON_3$ requires C, 66·3; H, 9·0; N, 17·85%); and the 2 : 4-*dinitrophenylhydrazone* formed red, microscopic, lath-shaped crystals (from aqueous dioxan), m. p. 217·5—219° (decomp.) after slight sintering (Found : N, 15·8. $C_{18}H_{22}O_4N_4$ requires N, 15·6%).

*γ-(2-Keto-4-methyl*cyclo*hexyl)valeric Acid.*—Ethyl γ-bromovalerate was prepared from γ-methylbutyrolactone (Staudinger and Ruzicka, *Helv. Chim. Acta*, 1924, **7**, 249), which was obtained by catalytic hydrogenation of lævulic acid (Schuette and Thomas, *J. Amer. Chem. Soc.*, 1930, **52**, 3010). The bromo-ester (20·4 g.) was heated on the water-bath for 50 hours with the potassio-compound from ethyl 5-methyl*cyclo*hexanone-2-carboxylate (Haworth, Mavin, and Sheldrick, J., 1934, 457) (18 g.) and potassium (3·9 g.) in benzene (120 c.c.). The reaction products were worked up in the usual way and gave 3·4 g. of the desired keto-ester (VIII), b. p. 153—156°/0·5 mm. The combined products from two batches were redistilled, and then heated at 100° for 20 hours with 5% aqueous potassium hydroxide (50 c.c.). From the alkaline solution was obtained 0·7 g. of a yellow liquid, b. p. about 160°/0·8 mm., which gave a crystalline *semicarbazone* of γ-(2-keto-4-methyl*cyclo*hexyl)valeric acid, m. p. 177—178·5° (Found : C, 57·5; H, 8·6. $C_{13}H_{23}O_3N_3$ requires C, 57·9; H, 8·6%).

*Attempted Simplification of the Conversion of γ-Δ^1-*cyclo*Hexenylbutyric Acid into 1-Decalone.*—Powdered anhydrous aluminium chloride (3·4 g.) was slowly added to a solution of γ-Δ^1-*cyclo*hexenylbutyryl chloride (see Part II) (from 2·1 g. of acid) in *cyclo*hexane (5 c.c.), cooled in a freezing mixture. The whole was then allowed to warm to room temperature; a vigorous reaction set in. When this had subsided, the mixture was heated at 70° until hydrogen chloride was no longer evolved. The product was worked up in the usual way, the only ketonic substance isolated being $\Delta^{9:10}$-1-octalone, identified by means of its semicarbazone and its 2 : 4-*dinitrophenylhydrazone*. An authentic specimen of the latter compound was prepared from $\Delta^{9:10}$-1-octalone obtained by the method described in Part II. It formed small, dark red, tabular crystals (from xylene), m. p. 266·5—267° (decomp.) (Found : N, 16·9. $C_{16}H_{18}O_4N_4$ requires N, 17·0%). For comparison, the 2 : 4-*dinitrophenylhydrazone* of *trans*-1-decalone was prepared. This formed small, thin, orange-red plates (from xylene), m. p. 222—222·5° (Found : N, 16·8. $C_{16}H_{20}O_4N_4$ requires N, 16·9%).

*Lactone of β-2-Hydroxy*cyclo*hexylpropionic Acid.*—β-2-Keto*cyclo*hexylpropionic acid was prepared by the method of Haworth and Mavin (J., 1933, 1015), and was further characterised by its *semicarbazone*, which separated from alcohol as a colourless crystalline powder, m. p. 181—182° (decomp.) (Found : N, 18·5. $C_{10}H_{17}O_3N_3$ requires N, 18·5%). The keto-acid (4 g.) was hydrogenated in alcoholic solution (80 c.c.) with platinum-black (0·5 g.). The product, b. p. 145°/10 mm., was the *lactone* of β-2-hydroxy*cyclo*hexylpropionic acid (Found : C, 69·7; H, 9·1. $C_9H_{14}O_2$ requires C, 70·1; H, 9·2%). Our contemplated conversion of this compound into 1-hydrindanone was rendered unnecessary by the publication of the experiments of Chuang *et al.* (*loc. cit.*), whose synthesis of 8-methyl-1-hydrindanone established the point in which we were interested—namely, that the intramolecular Darzens reaction could be utilised for the formation of a five-membered ring.

Methylation of trans-*1-Decalone.*

Finely powdered sodamide (3 g.) was gradually added to a solution of *trans*-1-decalone (7·5 g.) in anhydrous ether (50 c.c.), and the mixture then heated on the water bath for 1½ hours. After cooling, methyl iodide (11 g.) was slowly added, and then heating was continued for 3½ hours. Vigorous stirring was maintained throughout these operations. After addition of water, the ethereal solution was separated, washed, and dried (sodium sulphate), and the ether removed. The residue was treated with hydroxylamine hydrochloride and sodium acetate in boiling

aqueous-alcoholic solution, and the semi-solid mixture of oximes was fractionally crystallised from methyl alcohol. The predominating product was a crystalline oxime, m. p. 148—149·5°, not depressed by the oxime (m. p. 152—153·5°) of synthetic 2-methyl-1-decalone (see above). 2-Methyl-1-decalone (V), obtained by hydrolysis of this oxime, had b. p. 111°/12 mm., $n_D^{17°}$ 1·4812, $d_{4°}^{17°}$ 0·969; whence $[R_L]_D = 48·86$ (calc., 48·61) (Found: C, 79·2; H, 10·9. Calc.: C, 79·5; H, 10·9%). The semicarbazone of this ketone had m. p. 222—225° (decomp.), and did not depress the m. p. (216—217·5°) of the semicarbazone of synthetic 2-methyl-1-decalone (Found: N, 18·4. Calc.: N, 18·8%). Identification was completed by comparison of the 2 : 4-dinitrophenylhydrazones.

The more soluble fractions of the crystalline oximes of the methylated decalone gave a small amount of an *oxime* of a methyl-1-decalone, which crystallised from aqueous methyl alcohol in thin colourless needles, m. p. 139—139·5°, depressed to 133—134° by admixture with the oxime of synthetic 2-methyl-1-decalone (Found: C, 72·95; H, 10·4. $C_{11}H_{19}ON$ requires C, 72·8; H, 10·6%).

The mother-liquors from the first crystallisation of the oximes gave a gum which, after distillation (b. p. 155—156°/13 mm.), was hydrolysed, and the product treated with semicarbazide. Repeated crystallisation from methyl alcohol then gave a small amount of the semicarbazone of 9-methyl-1-decalone (IV), m. p. 223—224°, not depressed by a synthetic specimen.

The use of benzene instead of ether as a solvent in the methylation of *trans*-1-decalone led to substantially the same result.

Comparison of cis- *and* trans-*2-Decalones.*

The *cis*-2-decalone used in these experiments was prepared by chromic acid oxidation of *cis*-2-decalol, m. p. 105°, obtained by hydrogenation of *ar*-β-tetralol (prepared from tetralin by the method of Schroeter, *Annalen*, 1922, **426**, 119) in acetic acid solution with Adams's platinum catalyst at 4 atms.' pressure. For example, in one experiment, in which 115 g. of tetralol, 500 c.c. of acetic acid, and 2·5 g. of platinum oxide were used, hydrogenation was complete in 16 hours, and gave 37 g. of recrystallised *cis*-2-decalol. In all, 195 g. of the pure decalol were obtained from 475 g. of tetralol (compare Hückel, *Annalen*, 1926, **451**, 118).

3-*Chloro*-cis-2-*decalone* (XII).—A solution of chlorine (12 g.) in carbon tetrachloride (140 c.c.) was slowly added, with ice-cooling, to a solution of *cis*-2-decalone (25 g.) in carbon tetrachloride (40 c.c.), a trace of iodine being used for activation. After being kept at room temperature for an hour, the reaction mixture was washed with dilute sodium carbonate solution and water, dried (calcium chloride), and distilled at 10 mm. into fractions having b. p.'s 128—140°, 140—153°, 153—163°, and 163—173°. Crystals were eventually deposited by all four fractions, but in the case of the lowest fraction only after 3 weeks in the ice-chest. The crystals were drained free from oil, washed with light petroleum (b. p. 40—60°), and recrystallised from ligroin (b. p. 80—100°). 3-*Chloro*-cis-2-*decalone* (XII) (1·5 g.) formed long colourless needles, m. p. 107—108° (Found: C, 64·4; H, 8·2. $C_{10}H_{15}OCl$ requires C, 64·3; H, 8·1%).

3-*Hydroxy*-cis-2-*decalone*.—A suspension of the chloro-ketone (XII) (1·4 g.) in aqueous sodium hydroxide (0·4 g. in 25 c.c.) was boiled under reflux for an hour. After being kept overnight in the ice-chest, the crystals were collected and recrystallised from hot water. 3-*Hydroxy*-cis-2-*decalone* formed large, colourless, parallelogram-shaped crystals, m. p. 88—90° (Found: C, 71·5; H, 9·5. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·6%). The orientation was shown by oxidation of this hydroxy-ketone (0·5 g.) with a boiling solution of potassium permanganate (0·4 g.) in water (70 c.c.) to *cis*-*cyclo*hexane-1 : 2-diacetic acid, identified by comparison with a specimen prepared by direct oxidation of *cis*-2-decalol, m. p. 105° (Hückel, *Annalen*, **1925**, **441**, 17).

Ethyl cis-*2-Decalone-3-carboxylate*.—A mixture of *cis*-2-decalone (5 g.) and ethyl oxalate (5 g.), cooled to −15°, was slowly added to a solution of sodium ethoxide (0·8 g. of sodium in 16 c.c. of alcohol), also cooled to −15°. After being kept overnight in the ice-chest, the mixture was treated with ice-cold dilute sulphuric acid, and the oil extracted with ether. This ethyl *cis*-2-ketodecalyl-3-glyoxylate, which could not be obtained crystalline, was characterised by its 2 : 4-*dinitrophenylhydrazone*, ochre-coloured, microscopic, elongated plates which decomposed at 181—186° (Found: C, 55·35; H, 5·4. $C_{20}H_{24}O_7N_4$ requires C, 55·5; H, 5·6%). For conversion into *ethyl* cis-*2-decalone-3-carboxylate* the remainder of the crude glyoxylate was heated at 180° for an hour. The keto-ester (4·7 g.) formed a colourless liquid, b. p. 130°/0·7 mm., which gave an intense purple colour with ferric chloride in alcoholic solution (Found: C, 69·0; H, 9·0. $C_{13}H_{20}O_3$ requires C, 69·6; H, 9·0%). The 2 : 4-*dinitrophenylhydrazone* formed a yellow crystalline powder (from alcohol), m. p. 169—170·5° (decomp.) (Found: C, 56·6; H, 5·9; N, 13·6. $C_{19}H_{24}O_6N_4$ requires C, 56·4; H, 6·0; N, 13·9%).

Ethyl 3-Methyl-cis-*2-decalone-3-carboxylate* (XIII).—A solution of methyl iodide (5 g.) in methyl alcohol (15 c.c.) was added, with ice-cooling, to the sodio-compound prepared by addition of ethyl *cis*-2-decalone-3-carboxylate (5·4 g.) to sodium methoxide (0·55 g. of sodium in 15 c.c. of methyl alcohol). After being kept overnight in the ice-chest, the whole was heated on the water-bath until the methyl alcohol had distilled off, and the residue was extracted with ether and shaken twice with 15% potash solution. The extract was washed, dried (sodium sulphate), and distilled in a vacuum. *Ethyl 3-methyl*-cis-*2-decalone-3-carboxylate* (XIII) formed a colourless liquid (4·7 g.), b. p. 108·5—110°/0·4 mm., $n_D^{19°}$ 1·4879 (Found: C, 69·8; H, 9·2. $C_{14}H_{22}O_3$ requires C, 70·5; H, 9·3%). The substance gave a purplish coloration with ferric chloride in alcoholic solution, so a little of the unmethylated ester was probably still present. The 2 : 4-*dinitrophenylhydrazone* formed small yellow needles (from methyl alcohol), m. p. 120—121·5° (Found: C, 56·9; H, 6·1; N, 13·4. $C_{20}H_{26}O_6N_4$ requires C, 57·4; H, 6·3; N, 13·4%).

Dehydrogenation of the keto-ester (XIII) with selenium at 300—320° for 7 hours gave, in poor yield, 3-methyl-2-naphthol, which crystallised from dilute alcohol in almost colourless plates, m. p. 156·5—157° (Veselý and Štursa, *loc. cit.*, give 155—156°) (Found: C, 83·3; H, 6·5. Calc.: C, 83·5; H, 6·4%). 1-Methyl-2-naphthol, which would arise if condensation had occurred in position 1 of *cis*-2-decalone, has m. p. 110° (Fries and Hübner, *Ber.*, 1906, **39**, 441).

Ethyl 3-Methyl-trans-*2-decalone-3-carboxylate.*—In order to complete the comparison with the *cis*-compound, ethyl *trans*-2-decalone-3-carboxylate (Hückel and Goth, *loc. cit.*), which gave a 2 : 4-*dinitrophenylhydrazone* crystallising from alcohol in thin yellow needles, m. p. 181·5—182° (decomp.) (Found: C, 56·3; H, 6·0; N, 13·85. $C_{19}H_{24}O_6N_4$ requires C, 56·4; H, 6·0; N, 13·9%), was methylated as described for its *cis*-isomeride. The resulting *ethyl 3-methyl*-trans-*2-decalone-3-carboxylate* formed a colourless liquid, b. p. 113°/0·5 mm., which gave only a faint purple colour with alcoholic ferric chloride (Found: C, 69·2; 69·4; H, 9·2, 9·2. $C_{14}H_{22}O_3$ requires C, 70·5; H, 9·3%). The 2 : 4-*dinitrophenylhydrazone* formed small, hexagonal, orange plates (from methyl alcohol), m. p. 102·5—104° (Found: C, 57·2; H, 6·1; N, 13·4. $C_{20}H_{26}O_6N_4$ requires C, 57·4; H, 6·3; N, 13·4%). Selenium dehydrogenation of the methylated keto-ester gave 3-methyl-2-naphthol, in conformity with the orientation established by Hückel and Goth (*loc. cit.*) for ethyl *trans*-2-decalone-3-carboxylate.

2-β-*Phenylethyl*-cis-*2-decalol.*—*cis*-2-Decalone (10 g.), diluted with ether (20 c.c.), was added to an ice-cold Grignard solution prepared from β-phenylethyl chloride (10·8 g.), magnesium turnings (2 g.), and anhydrous ether (80 c.c.). After being kept at 0° for an hour and then at room temperature for an hour, the mixture was heated under reflux for 2 hours and then decomposed with ice and ammonium chloride. The ethereal solution was washed, dried (sodium sulphate), and distilled. The distillate (10·1 g.), b. p. 165—168°/0·5 mm., solidified on cooling, and was recrystallised from ligroin. 2-β-*Phenylethyl*-cis-*2-decalol* (4·7 g.) formed small colourless plates, m. p. 111—112° (Found: C, 83·4; H, 10·1. $C_{18}H_{26}O$ requires C, 83·7; H, 10·15%). Dehydration of the crystalline carbinol (4·2 g.) with potassium hydrogen sulphate (8·5 g.) at 170—180° (2½ hours) gave 2-β-*phenylethyl*-cis-$\Delta^{2:3}$-*octalin* (XIV) (3·4 g.), a colourless liquid, b. p. 148—149°/0·9 mm., $n_D^{16·7°}$ 1·5449 (Found: C, 89·7; H, 10·0. $C_{18}H_{24}$ requires C, 89·9; H, 10·1%).

Cyclisation of 2-β-*Phenylethyl*-cis-$\Delta^{2:3}$-*octalin.*—Finely powdered anhydrous aluminium chloride (4·5 g.) was slowly added to an ice-cold solution of the unsaturated hydrocarbon (XIV) (3·6 g.) in carbon disulphide (35 c.c.). After being kept for 3 hours at 0° and then overnight at room temperature, the mixture was decomposed with ice, and the carbon disulphide solution was washed, dried (calcium chloride), and distilled. The distillate (3·0 g.), b. p. 154°/0·5 mm., deposited crystals when kept in the ice-chest overnight. These were collected, drained on a tile, and recrystallised from methyl alcohol. They had m. p. 68—70°, not depressed by the dodecahydro-1 : 2-benzanthracene similarly prepared from *trans*-2-decalone (Cook and Hewett, *loc. cit.*).

Dehydrogenation of Saturated Hydrocarbons obtained by Cyclisation of (XIV).—(i) The liquid mixture from which the crystalline dodecahydrobenzanthracene had been separated was heated at 300—320° for 7½ hours with platinum-black. The products were extracted with benzene, and the filtered solution was concentrated and treated with alcohol. Crystals separated and these were extracted with boiling alcohol to which a little benzene had been added. A few mg. of material remained undissolved; this, after recrystallisation from benzene, was shown to be chrysene by direct comparison of the hydrocarbon and its 2 : 7-dinitroanthraquinone complex with authentic specimens. The alcohol–benzene liquors gave crystals, m. p. 123—124°, after repeated crystallisation. This product was identical with the octahydrobenzanthracene described under (ii) (Found: C, 90·9; H, 8·4%); when dehydrogenated with selenium at 340—

360°, it gave 1 : 2-benzanthracene, identified by comparison of the hydrocarbon and its 2 : 7-dinitroanthraquinone complex with authentic specimens. The 2 : 7-*dinitroanthraquinone complex* of 1 : 2-benzanthracene, which has not been described hitherto, crystallises from xylene in magenta needles, m. p. 252—253° (decomp.) (Found : C, 73·1; H, 3·4. $C_{18}H_{12},C_{14}H_6O_6N_2$ requires C, 73·0; H, 3·4%).

(ii) Without separating the crystalline dodecahydro-1 : 2-benzanthracene, we heated the distilled mixture of saturated hydrocarbons (2·2 g.) at 300—305° for 5½ hours with palladium-black. About 500 c.c. of hydrogen were liberated. 1 : 2-Benzanthracene (0·6 g.) was isolated from the product by crystallisation from alcohol. The m. p.'s of this hydrocarbon (165—167°; lit., 160°) and its picrate (138—139°; lit., 141·5—142·5°) showed that it was not quite pure; doubtless the contaminant was chrysene, which is much less soluble. In order to remove the last traces of benzanthracene, the oil remaining after removal of the alcohol from the mother-liquors was refluxed for 1½ hours with maleic anhydride (1 g.) in xylene (20 c.c.). 2*N*-Sodium hydroxide (25 c.c.) was then added, the xylene distilled in steam, and the gum extracted and treated in alcoholic solution with picric acid (1·5 g.). The crystalline picrates were recrystallised from alcohol. The first crop formed orange needles, m. p. 150—151°, not depressed by the picrate of tetrahydrobenzanthracene (m. p. 155°; Cook and Hewett, *loc. cit.*). On standing in the ice-chest for 2 days, the mother-liquors deposited light red needles; these were freed from picric acid, and the resulting hydrocarbon recrystallised from alcohol. This *octahydro*-1 : 2-*benzanthracene* (XVII) formed slender colourless needles, m. p. 124·5—125·5° (Found : C, 91·0; H, 8·5. $C_{18}H_{20}$ requires C, 91·45; H, 8·55%). Examination of the mother-liquors from the crystallisation of the picrates did not reveal the presence of any other constituent; there was no indication of 3 : 4-benzphenanthrene, which forms a characteristic, rather sparingly soluble, red picrate (Cook, J., 1931, 2524).

3-*Keto*-Δ^4-*hexadecahydro*-1 : 2-*benzanthracene* (XVIII; trans-*form*).—The sodio-compound of *trans*-2-decalone (5 g.) was prepared by stirring its solution in anhydrous ether (50 c.c.) with finely powdered sodamide (1·3 g.) for 7 hours, the whole being finally refluxed for ½ hour. The ice-cold suspension was then treated slowly with acetyl-Δ^1-*cyclo*hexene (4·1 g.). After being kept at room temperature overnight, the mixture was boiled for an hour, then cooled, and decomposed with dilute sulphuric acid. The ethereal layer was washed, dried (sodium sulphate), and distilled. The fraction (3·3 g.), b. p. 192—195°/1·3 mm., gave a *semicarbazone*, which separated from aqueous dioxan as a colourless microcrystalline powder, m. p. 240·5—241·5° (decomp.) (Found : C, 72·3; H, 9·7. $C_{19}H_{29}ON_3$ requires C, 72·3; H, 9·3%), and a 2 : 4-*dinitrophenylhydrazone*, which formed small reddish-orange needles (from aqueous dioxan), m. p. 201·5—204° (decomp.) (Found : C, 65·5; H, 7·0. $C_{24}H_{30}O_4N_4$ requires C, 65·7; H, 6·9%). The ketone (XVIII; *trans*-form) obtained by hydrolysis of the semicarbazone was a viscous oil which began to crystallise after a month. When dehydrogenated with selenium at 300—320°, it gave 1 : 2-benzanthracene.

3-*Keto*-Δ^4-*hexadecahydro*-1 : 2-*benzanthracene* (XVIII; cis-*form*).—The sodio-derivative of *cis*-2-decalone (10 g.) was treated with acetyl-Δ^1-*cyclo*hexene as described for the *trans*-compound, and yielded 7·5 g. of a fraction, b. p. 184—189°/0·6 mm. This distillate deposited crystals of 3-*keto*-Δ^4-*hexadecahydro*-1 : 2-*benzanthracene* (XVIII; *cis*-form), which were separated from oil, drained on a tile, and recrystallised from ligroin; they formed small colourless needles, m. p. 122—122·5° (Found : C, 83·4; H, 9·95. $C_{18}H_{26}O$ requires C, 83·7; H, 10·15%). The *semicarbazone*, prepared from the crude distilled ketone, crystallised from aqueous dioxan in microscopic prisms, m. p. 258·5° (decomp.) (Found : C, 72·3; H, 9·3. $C_{19}H_{29}ON_3$ requires C, 72·3; H, 9·3%), and the 2 : 4-*dinitrophenylhydrazone* crystallised from dioxan–alcohol in orange-red microscopic needles, m. p. 172·5—179° (decomp.) (Found: C, 65·5; H, 6·9. $C_{24}H_{30}O_4N_4$ requires C, 65·7; H, 6·9%). Hydrolysis of the semicarbazone by boiling dilute sulphuric acid gave the same crystalline ketone which had been separated from the crude mixture, and the structure of this ketone was established by its dehydrogenation to 1 : 2-benzanthracene by selenium at 300—320°.

In another experiment the mixture of ketones (3·8 g.; b. p. 165—175°/0·5 mm.) from *cis*-2-decalone (5 g.) and acetyl-Δ^1-*cyclo*hexene (4·1 g.) was reduced by 6 hours' boiling with acetic acid (50 c.c.), concentrated hydrochloric acid (50 c.c.), and amalgamated zinc wool (15 g.). At the end of the first hour toluene (10 c.c.) and concentrated hydrochloric acid (10 c.c.) were added, further portions of hydrochloric acid (10 c.c.) being then added after each hour. The product (b. p. 136—138°/0·6 mm.; 3·2 g.) was heated with platinum-black (0·25 g.) at 300—320° for 7 hours. 1 : 2-Benzanthracene (0·45 g.) was isolated by crystallisation from alcohol. In order to remove the last traces of this hydrocarbon the material recovered from the mother-

liquors was refluxed for 2 hours with maleic anhydride (2 g.) in xylene (15 c.c.). The xylene was removed in steam in presence of excess of alkali, and the residual oil was extracted with ether, and then, after removal of the ether, treated with alcoholic picric acid. Fractional crystallisation of the picrates gave a small amount of the picrate of tetrahydro-1 : 2-benzanthracene, identified by the method of mixed m. p.'s, and an impure specimen of the picrate of 3 : 4-benzphenanthrene (0·3 g.; m. p. 118—120°; lit., 126—127°). The hydrocarbon regenerated from this picrate was identified by comparison with authentic 3 : 4-benzphenanthrene and by oxidation to the quinone, and conversion of this into the corresponding phenazine. The m. p.'s of these derivatives were not depressed by admixture with authentic specimens (Cook, J., 1931, 2524).

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169. *The Constitution and Reactions of Thiocarbonyl Tetrachloride. Part III. Reaction with Primary Alkylamines and Phenols.*

By Joseph M. Connolly and G. Malcolm Dyson.

S-Aryloxytrichloromethylthiols, obtained by the action of thiocarbonyl tetrachloride on sodium phenoxides (Connolly and Dyson, J., 1935, 679), have been further investigated. *S*-Phenoxytrichloromethylthiol in ethereal solution with sodium ethoxide (1 mol.) in dry ethyl alcohol gives sodium phenoxide and a yellow oil. Since no sodium chloride separates, the trichloromethyl group is unaffected, an interchange of groups taking place :

$$C_6H_5{\cdot}O{\cdot}S{\cdot}CCl_3 + EtONa = EtO{\cdot}S{\cdot}CCl_3(I) + C_6H_5{\cdot}ONa$$

S-Ethoxytrichloromethylthiol (I) yields thiocarbonyl tetrachloride and alcohol with dry hydrogen chloride in dry ether, and *s*-triphenylguanidine hydrochloride with aniline in ligroin. It was synthesised from thiocarbonyl tetrachloride and one molecular proportion of sodium ethoxide : $EtONa + CCl_3{\cdot}SCl = (I) + NaCl$. *S*-Alkoxytrichloromethylthiols, with excess of the corresponding sodium alkyloxide in dry alcohol, form tetra-alkyl esters of orthocarbonic acid :

$$(I) + 3NaOEt \longrightarrow EtO{\cdot}S{\cdot}C(OEt)_3 + 3NaCl \longrightarrow 3NaCl + C(OEt)_4 + Na_2S$$

The yields are higher than those obtainable by other methods (*e.g.*, chloropicrin).

Thiocarbonyl tetrachloride reacts on primary alkylamines as on primary arylamines, giving *S*-alkylaminotrichloromethylthiols. These are pale yellow oils decomposing spontaneously on standing, though not as rapidly as the corresponding aryl derivatives. They are similar in properties to the latter (Connolly and Dyson, J., 1934, 822; 1935, 679), except that hydrolysis with hydrochloric acid chiefly yields the amine hydrochloride and little thiocarbimide. Compounds analogous to the tetrachlorodiaryltetrahydrodithiapyrazines cannot be obtained by treating the thiols with alcoholic potash. Treatment with the corresponding alkylamine in ligroin solution yields the trialkylguanidine hydrochloride. This is a new method for the synthesis of trialkylguanidine hydrochlorides, specimens of which for comparison were prepared by another method, *s*-dialkylthiourea being converted into the sulphate of its methyl derivative by methyl sulphate and into the trialkylguanidine sulphate by a further molecular proportion of the amine, followed by conversion into the guanidine base, then into its hydrochloride :

$$2CS(NHR)_2 \xrightarrow{Me_2SO_4} [NHR{\cdot}C(SMe){:}NR]_2SO_4 \xrightarrow{2NH_2R} [NR{:}C(NHR)_2]_2SO_4 + 2MeSH$$

Experimental.

n-*Heptylamine*.—*n*-Heptaldoxime (258 g.) in dry alcohol (4 l.) was placed in a 12 l. three-necked flask fitted with twin 180 cm. reflux condensers. Sodium (500 g.) was added in large pieces through the centre neck as rapidly as possible, consistent with safety. After the reduction, water (6 l.) was added slowly, and the mixture distilled, 9 l. of the distillate being collected in 50% hydrochloric acid (600 ml.). The acid distillate was concentrated to 700 ml. under reduced pressure and treated with 40% potash solution (1 l.) and the amine layer was separated, dried over caustic potash, and distilled; the *n*-heptylamine (127 g.) obtained had b. p. 154°.

*iso*Amylamine, b. p. 94—97°, was prepared similarly from *iso*valeraldoxime.

Allylamine, b. p. 53°, was prepared by the hydrolysis of allylthiocarbimide with boiling 30% hydrochloric acid.

S-n-*Heptylaminotrichloromethylthiol.*—*n*-Heptylamine (3·5 g.) in ether (10 ml.) was added to a stirred mixture of anhydrous potassium carbonate (2 g.) in water (50 ml.) and thiocarbonyl tetrachloride (5 g.) in ether (20 ml.). After 15 minutes, the ethereal layer was removed, washed twice with *N*-hydrochloric acid and once with water, and dehydrated over anhydrous potassium carbonate, and the ether removed in a vacuum at room temperature. The chlorothiol, an almost colourless oil with a geranium-like odour, decomposed spontaneously on standing and violently on heating to 170°.

The corresponding allyl compound, prepared by the same method, was also an unstable oil, decomp. 170°.

Triallylguanidine Hydrochloride.—*S*-Allylaminotrichloromethylthiol was prepared in ligroin solution by adding allylamine (3 g.) to thiocarbonyl tetrachloride (5 g.) in ligroin (100 ml.). Allylamine (6 g.) was then added, and the mixture boiled under reflux for 9 hours. After cooling, the ligroin layer was decanted, and the residue extracted with dilute hydrochloric acid. The extract, on concentration, yielded colourless rhombs of *triallylguanidine hydrochloride*, m. p. and mixed m. p. (with a specimen prepared by another method) 176° (Found: Cl, 16·8. $C_{10}H_{17}N_3$,HCl requires Cl, 16·5%).

The *tribenzyl* and the *triisoamyl* analogue, prepared by the same method, were colourless microcrystalline powders, m. p. 201° and 206° respectively (Found for the former: Cl, 9·4. $C_{22}H_{23}N_3$,HCl requires Cl, 9·7%. Found for the latter: Cl, 12·0. $C_{16}H_{35}N_3$,HCl requires Cl, 11·6%).

Tribenzylguanidine Hydrochloride (*Method* II).—Benzylamine (4 g.) in chloroform (40 ml.) was converted into benzylthiocarbimide by shaking with thiocarbonyl chloride (3·7 g.) and water (150 ml.) for 15 minutes. The chloroform layer was removed, washed with water, and boiled with benzylamine (4 g.) for 30 minutes. On evaporation, *s*-dibenzylthiourea, a white microcrystalline powder, was obtained. This was methylated by gentle boiling for 1½ hours with methyl sulphate (0·9 g.) and water (1 ml.). Benzylamine (1·4 g.) was then added, and the mixture heated on a water-bath for 9 hours. Methylthiol was evolved and the mixture solidified. The solid was extracted with hot water; the extract on cooling yielded crystals of tribenzylguanidine sulphate. These were removed, dissolved in hot water, and made alkaline with caustic soda, and the liberated base (an oil) extracted with ether. The ethereal extract was washed with water, shaken with concentrated hydrochloric acid, and diluted, and the ether evaporated. Tribenzylguanidine hydrochloride separated, on cooling, as a microcrystalline powder, m. p. 203°.

The triallyl and the tri*iso*amyl analogue were prepared by the same method as white crystalline powders, m. p. 176° and 205° respectively.

S-*Ethoxytrichloromethylthiol.*—*S*-Phenoxytrichloromethylthiol, prepared from thiocarbonyl tetrachloride (40 g.) in dry ether (200 ml.) (*loc. cit.*), was shaken with a solution of sodium (6 g.) in dry ethyl alcohol (100 ml.). After 7 minutes, the mixture was shaken with water (700 ml.) to remove alcohol and sodium phenoxide, and ether (30 ml.) was added. The extract was dried (anhydrous potassium carbonate) and evaporated in a vacuum at room temperature. The residual *S*-ethoxytrichloromethylthiol was washed with water, dried, and obtained as a yellow oil with a pungent fruity odour, b. p. 155° (decomp.). It was also prepared by adding thiocarbonyl tetrachloride (18·6 g.) in dry ether (100 ml.) to sodium (3 g.) in dry ethyl alcohol (50 ml.); after 7 minutes, the mixture was poured into water, and the product isolated as before as a pale yellow oil, b. p. 160° (decomp.).

Tetraethyl Orthocarbonate.—To a solution of sodium (15 g.) in dry ethyl alcohol (240 ml.) in a flask fitted with a reflux condenser was added thiocarbonyl tetrachloride (20 g.) in dry ether (100 ml.). *S*-Ethoxytrichloromethylthiol was first formed and this then reacted violently with the excess of sodium ethoxide, sodium chloride being precipitated. After 4 hours, the mixture was poured into water (1 l.) and extracted twice with ether (160 ml.). Removal of the ether from the dried extract (calcium chloride) left a residue (10 g.), from which, on fractionation, tetraethyl orthocarbonate (8 g.) was obtained as a colourless liquid, b. p. 158°, $d_{4^\circ}^{17^\circ}$ 0·916. Hydrolysis with 80% potash solution yielded potassium carbonate and ethyl alcohol.

*S-iso*Butoxytrichloromethylthiol, a colourless oil, b. p. 181° (decomp.)/760 mm., in reaction with sodium *iso*butoxide, yielded tetra*iso*butyl orthocarbonate as a pale yellow oil, b. p. 238°.

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170. *Isomerisation of 2 : 3-Dimethyl Ascorbic Acid.*

By W. N. HAWORTH, E. L. HIRST, F. SMITH, and W. J. WILSON.

THE physical and chemical properties of ascorbic acid (I), 3-methyl ascorbic acid (II), 2 : 3-dimethyl ascorbic acid (III), and 2 : 3 : 5 : 6-tetramethyl ascorbic acid (Haworth, Hirst, and Smith, J., 1934, 1556) show that each of these substances contains the normal ring system of ascorbic acid (Herbert, Hirst, Percival, Reynolds, and Smith, J., 1933, 1270). It is clear also that when 2 : 3-dimethyl ascorbic acid is made to react with alkali the product is the salt of the open-chain acid (IV), the only unexpected observation at this stage being the loss of selective absorption when the lactone ring is opened. What has hitherto been by no means certain is the structure of the product formed when the salt (IV) is acidified by addition of mineral acid. We have shown previously that it is possible to regenerate 2 : 3-dimethyl ascorbic acid directly from the acid so formed and this we have been able to confirm (see later). But subsequent work by Micheel (*Annalen*, 1935, **519**, 70; 1936, **525**, 66) has revealed that direct regeneration of dimethyl ascorbic acid is not the normal course of the reaction and that the product usually obtained consists mainly of a structural isomeride of dimethyl ascorbic acid characterised by absence of selective absorption and by the possession of only one free hydroxyl group. As the result of these and other experiments with 6-trityl dimethyl ascorbic acid, which showed that a free hydroxyl group at C_6 was necessary for the occurrence of isomerisation, Micheel suggested various structural formulæ. Of these he considered (XI) and (V) to be the most likely and indicated a definite preference for (XI). Our experiments on the other hand lead us to the conclusion that (V) best represents the properties of iso*dimethyl ascorbic acid*.

By repetition of our earlier experiments we have confirmed the observation that under certain conditions regeneration of 2 : 3-dimethyl ascorbic is possible from the product obtained on acidification of (IV). The presence of some catalyst is probably necessary and somewhat drastic conditions are required. Under ordinary conditions the product is always the *iso*dimethyl ascorbic acid. The latter substance reacts readily with alcoholic ammonia, giving almost quantitatively the amide, $C_8H_{15}O_6N,CH_3{\cdot}OH$ (m. p. 120°), which is obtainable also, but with greater difficulty and in smaller yield, from ordinary dimethyl ascorbic acid. We have previously commented on the unexpected resistance of this amide to ozonisation and further peculiarities have now been observed. For instance it loses ammonia very readily and in cold methyl-alcoholic solution it undergoes transformation with change of rotation and production of a substance showing strong absorption at λ2300 A., indicating the re-establishment of the true ascorbic acid structure. It is possible, therefore, that the amide may have the structure (VI*b*) or (VI*c*) instead of (VI*a*) as formerly supposed. With sodium hydroxide it reacts normally, giving the salt (IV).

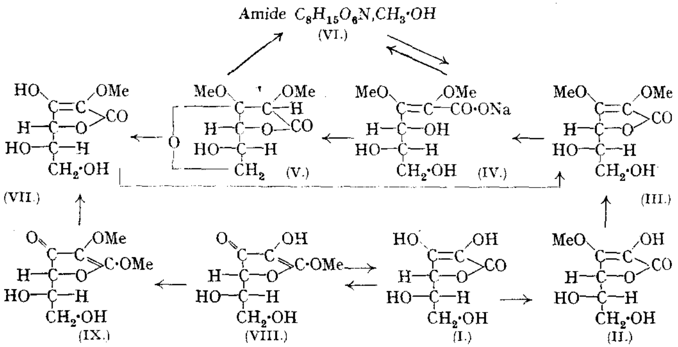
Inspection of the formula (V) reveals that the methoxyl group at C_3 is in reality glucosidic in type and is present in a ring system which is decidedly strained. It is to be expected, therefore, that this group would be labile in character and experiments show that this is indeed the case.

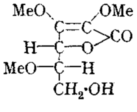
When boiled with methyl-alcoholic hydrogen chloride, *iso*dimethyl ascorbic acid gives a monomethyl ascorbic acid which has the true ascorbic acid structure. This substance has reducing properties, shows the type of absorption spectrum characteristic of ascorbic acid, and reacts smoothly with diazomethane, giving 2 : 3-dimethyl ascorbic acid. It differs from the known 3-methyl ascorbic acid in not giving a blue colour with ferric chloride and it must therefore be 2-*methyl ascorbic acid*.

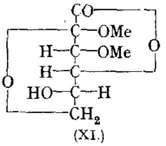
Further information on this point is forthcoming from another source. When ascorbic acid reacts with one molecular proportion of diazomethane, two products can be isolated. One of these is the normal 3-methyl ascorbic acid, but the other possesses an absorption spectrum and a rotation value which indicate that it differs structurally from ascorbic acid. It was named tentatively 2(?)-methyl ascorbic acid (Haworth, Hirst, and Smith, J., 1934, 1560), but it now seems probable that it is the 1-methyl derivative (VIII) of one of the several possible tautomeric modifications of ascorbic acid and we propose to name it 1-methyl hetero-ascorbic acid. It loses methyl alcohol in cold aqueous solution, ascorbic

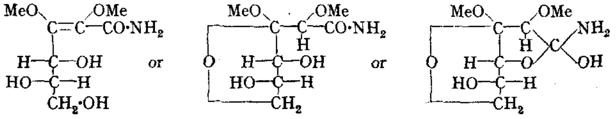
acid being regenerated. On methylation with diazomethane its structure remains unaltered and it yields a dimethyl derivative (IX) which again loses methyl alcohol in cold aqueous solution. The product is a monomethyl derivative which possesses the ordinary ascorbic acid structure and is identical with the monomethyl ascorbic acid (VII) derived from *iso*-dimethyl ascorbic acid by the action of methyl-alcoholic hydrogen chloride. There appears to be no question of enolisation involving a double bond between C_3 and C_4, since this would destroy the dissymmetry of C_4 and the products obtained from methyl hetero-ascorbic acid would in that event be expected to consist of derivatives of both ascorbic acid and its stereoisomeride, araboascorbic acid : only the former are found. No structure involving the usual double bond between C_2 and C_3 is possible and consequently we formulate methyl hetero-ascorbic acid with the double bond between C_1 and C_2 The labile methyl group in both the mono- and the di-methyl derivative of hetero-ascorbic acid must be on C_1, since hydrolysis of the dimethyl derivative gives 2-methyl ascorbic acid.

In the case of (VIII) and (IX) loss of the methyl group at C_1 results in rearrangement and re-formation of the valency system present in normal ascorbic acid. Such a reaction is by no means unusual and the most unexpected feature of the present series of experiments lies in the transformation from (IV) to (V) when lactonisation is accompanied by a second ring formation brought about by the saturation of the double bond between C_2 and C_3 by the hydroxyl group on C_6. Similar reactions have been recorded in the case of 2-carboxylic acids, but in the present instance the transformation is reversible. It appears, however,




(X.)


(XI.)



(VI*a*.) (VI*b*.) (VI*c*.)

that carlic acid (Clutterbuck, Raistrick, and Reuter, *Biochem. J.*, 1935, 873) provides a close analogy, for when the hydrated form of carlic acid is lactonised an additional ring is formed as the result of saturation of the double bond of the tetronic acid residue by a side-chain hydroxyl group. The reaction is reversible, the double bond being re-formed on hydration (for further comments on this reaction see Haworth, Hirst, and Jones, this vol., p. 549).

Micheel has already shown that the formation of the saturated *iso*-derivative does not take place if a triphenylmethyl ether group is substituted for the hydroxyl group at C_6. We have confirmed this, and also his observation that 6-trityl dimethyl ascorbic acid exists in two forms, and have further shown that isomerisation involves interaction between the double bond and the hydroxyl group at C_6.

The various reactions studied are summarised in the preceding schemes. In addition to the cycles of changes shown, transformations indicated by the stages (III)⟶(IV)⟶(V)⟶(VI) and (V)⟶(VII)⟶(III) have been completed also with 2 : 3 : 5-trimethyl ascorbic acid (X) as starting substance.

EXPERIMENTAL.

iso*Dimethyl* l-*Ascorbic Acid.*—In the following experiments crystalline dimethyl ascorbic acid, m. p. 63°, was employed as starting material. This can be obtained most conveniently by methylation of 3-methyl ascorbic acid with diazomethane (Haworth, Hirst, and Smith, *loc. cit.*). Direct transformation of ascorbic acid into the dimethyl derivative is also possible, but this procedure gives a product which crystallises more slowly. When dimethyl ascorbic acid was allowed to react with dilute barium hydroxide (1 mol. being taken up), the rotation changed to $[\alpha]_D^{20°}$ − 21° (concentration calculated on weight of dimethyl ascorbic acid), and the solution then displayed no selective absorption in the ultra-violet. The excess of barium hydroxide was removed by passing carbon dioxide, and the barium present as salt of the open-chain acid was exactly precipitated as sulphate by titration with dilute sulphuric acid. At this stage the rotation had the constant value − 14° and the solution showed only slight general absorption. Concentration of the solution under diminished pressure in absence of air left a stiff colourless syrup, which was slightly acid to litmus but titrated as a lactone. Its rotation varied in different experiments between $[\alpha]_D^{20°}$ − 10° and $[\alpha]_D^{20°}$ − 15° (both values in methyl alcohol). Usually it displayed no selective absorption, but occasionally a weak band at λ2300 A. was observed, the intensity of which corresponded to the presence of *ca.* 5% by weight of dimethyl ascorbic acid.

Purification of iso*dimethyl ascorbic acid* was effected by distillation in a high vacuum, b. p. 175°/0·03 mm. (bath temp.), $n_D^{18°}$ 1·4795, $[\alpha]_D^{22°}$ − 18° in methyl alcohol (*c*, 2·0). No selective absorption (Found: C, 46·8; H, 6·0; OMe, 30·3; equiv., by titration, 210. $C_8H_{12}O_6$ requires C, 47·0; H, 5·9; OMe, 30·4%; equiv., 204). The substance was non-reducing, behaved as a lactone, and readily gave the mono-*p*-nitrobenzoate, m. p. 180°, $[\alpha]_D^{21°}$ + 19° in chloroform (*c*, 1·7), described by Micheel (*loc. cit.*). Furthermore, on treatment with methyl-alcoholic ammonia, *iso*dimethyl ascorbic acid gave readily and in almost theoretical yield (contrast dimethyl ascorbic acid, which gives under similar conditions a yield of 25%), the amide $C_8H_{15}O_6N,CH_3{\cdot}OH$, m. p. 120° (Micheel and Kraft, *Z. physiol. Chem.*, 1933, **215**, 222; Herbert, Hirst, Percival, Reynolds, and Smith, *loc. cit.*) (Found: C, 42·7; H, 7·6; N, 5·3; OMe, 33·6. Calc. for $C_8H_{15}O_6N,CH_3{\cdot}OH$: C, 42·7; H, 7·5; N, 5·5; OMe, 36·8%).

When the amide (0·35 g.) was warmed with *N*/5-barium hydroxide at 60°, in an atmosphere of nitrogen, ammonia was evolved. When no more ammonia came over, carbon dioxide was passed to remove the excess of barium hydroxide. The solution now showed $[\alpha]_D$ − 16° (calc. on weight of amide used). A slight deficiency of sulphuric acid was added to remove almost all the barium and the solution was evaporated under reduced pressure. The syrup was dissolved in methyl alcohol, and ether added to precipitate the small remaining amount of barium salt. Evaporation of the solution then gave a syrup, $[\alpha]_D^{16°}$ − 14° in methyl alcohol (*c*, 1·7), which readily gave the mono-*p*-nitrobenzoate, m. p. 180°, and from which the amide, m. p. 120°, could easily be regenerated. The syrup did not display selective absorption. It was therefore *iso*dimethyl ascorbic acid (Found: OMe, 30·6. Calc., 30·4%).

It was found also that the amide, although stable in cold aqueous solution, decomposes in boiling water with evolution of ammonia. After elimination of the ammonia and isolation of the product, *iso*dimethyl ascorbic acid was obtained. A solution of the amide in methyl alcohol had the initial value, $[\alpha]_D^{16°}$ − 24°, but the value was not constant and reached + 3° at the end of 3 days. The original solution showed no selective absorption (tested after dilution with methyl

alcohol such that the concentration was 10 mg. per 100 c.c.), but the final solution showed a strong absorption band at λ2300 A. (ε = 4000). It was observed also that when the amide was recrystallised from methyl alcohol, the mother-liquors had a positive rotation. It seems, therefore, that some transformation (possibly reversion to 2 : 3-dimethyl ascorbic acid) takes place in methyl alcohol and this may account for the observation that it is very difficult to raise the m. p. of the amide beyond 120° by recrystallisation from methyl alcohol. Samples which require little purification have m. p. 124°, as previously recorded.

Transformation of iso*Dimethyl Ascorbic into Dimethyl Ascorbic Acid.*—The direct transformation takes place somewhat capriciously. We have previously reported the regeneration of dimethyl ascorbic acid by heating the isomeric substance at 120°/0·1 mm. We have not been able to repeat this on all occasions, but in some experiments simple heating in a vacuum has resulted in regeneration of dimethyl ascorbic acid (yield, 80%). It is possible, however, that some catalyst was present, since specially purified and acid-free samples of *iso*dimethyl ascorbic acid could not be transformed in this way.

Action of Methyl-alcoholic Hydrogen Chloride on iso*Dimethyl Ascorbic Acid.*—It was shown in preliminary experiments that dimethyl ascorbic acid is recovered unchanged after being boiled for several hours with 3% methyl-alcoholic hydrogen chloride. When *iso*dimethyl ascorbic acid (2 g.) was boiled with 3% methyl-alcoholic hydrogen chloride for 12 hours, the rotation changed from $[\alpha]_D^{20°}$ − 14° to + 40° and a strong absorption band at λ2400 A. (ε = 8000) made its appearance. The solution was then divided into two portions, A and B (100 c.c. each). To the first portion (A) excess of an ethereal solution of diazomethane was added. After 24 hours at − 10° the solvent was removed, and the product extracted with ether containing a little water. On concentration of the ethereal solution the hydrate of dimethyl ascorbic acid crystallised, m. p. 59°, $[\alpha]_D^{23°}$ + 32° in methyl alcohol (*c*, 0·5) (Found : OMe, 27·5. Calc., 27·9%). It gave a di-*p*-nitrobenzoate, m. p. 171°, and on treatment with ammonia in methyl alcohol it gave (in the usual moderate yield) the amide, m. p. 119°.

The other portion (B) of the above solution was neutralised with barium carbonate. The neutral solution was evaporated to dryness, and the organic material dissolved in acetone. Removal of the acetone left a syrup, which was acidic and strongly reducing and gave a red colour with methyl-alcoholic ferric chloride. Its aqueous solution showed a strong absorption band at λ2450 A. (ε, 5000) (band at λ2600 A. in dilute alkali; ε, 6500). It consisted mainly of 2-*methyl ascorbic acid*, $[\alpha]_D$ + 10° in water (*c*, 1·5) (Found : OMe, 16·4. $C_7H_{10}O_6$ requires OMe, 16·3%). On methylation with diazomethane in the usual manner the monomethyl derivative gave quantitatively a syrup which had OMe 28%, $[\alpha]_D^{19°}$ + 23° in methyl alcohol (*c*, 0·3), showed a strong absorption band at λ2350 A. in aqueous solution, and gave the amide, m. p. 119°, on treatment with methyl-alcoholic ammonia. The syrup was extracted with ether, and the solution concentrated until a slight turbidity appeared. On cooling this solution, 2 : 3-dimethyl *l*-ascorbic acid monohydrate was deposited. This had m. p. 58°, $[\alpha]_D$ + 28° in water (*c*, 0·5), and an absorption band at λ2350 A. (ε, 10,000) which disappeared on addition of alkali. It was therefore mainly dimethyl ascorbic acid.

Monomethyl Hetero-ascorbic Acid (1 ?-*Methyl*).—It has already been shown (J., 1934, 1560) that methylation of ascorbic acid with diazomethane gives in small yield (besides 3-methyl ascorbic acid) another monomethyl derivative which has unusual properties and was provisionally named 2(?)-methyl ascorbic acid. This was prepared by the method described and had m. p. 162°, $[\alpha]_D^{20°}$ + 240° in methyl alcohol (*c*, 0·5), and showed in aqueous solution an intense absorption band at λ2800 A. (λ3200 A. in dilute alkali). An aqueous solution had $[\alpha]_D^{20°}$ + 200° (*c*, 1·5), but this value slowly fell to + 28° when the solution was kept at room temperature. Evaporation of the water at 40° in an atmosphere of nitrogen left *l*-ascorbic acid, m. p. 185° (no depression when mixed with an authentic sample of m. p. 189°) (Found : OMe, nil). The identity of the substance was confirmed by chemical and crystallographic examination.

Methylation of the methyl hetero-ascorbic acid with diazomethane gave the syrupy dimethyl derivative, $[\alpha]_D^{20°}$ + 107° in methyl alcohol; band at λ2700 A. in water (ε, 7000) (see J., 1934, 1560). When an aqueous solution of the dimethyl derivative was kept at 50° under nitrogen, the rotation decreased to + 9° and on removal of the water in an atmosphere of nitrogen (diminished pressure) a strongly acidic syrup was obtained which gave a red colour with methyl-alcoholic ferric chloride and showed an absorption band at λ2400—2450 A. in water (ε, 3600) (λ2600 A. in dilute alkali; ε, 4600), $[\alpha]_D^{19°}$ + 13° in water (*c*, 0·8) (Found : OMe, 21·0. Calc. for monomethyl ascorbic acid : OMe, 16·3%). It appeared to be mainly 2-methyl ascorbic acid (see above) and on methylation with diazomethane it gave syrupy 2 : 3-dimethyl ascorbic acid [band at λ2350 A. in water (ε, 5100), disappearing on addition of alkali] (Found : OMe, 28·9%).

The syrup was extracted with boiling ether and treated with light petroleum to give a turbid solution. After the latter had been kept for several hours at − 5°, crystalline 2 : 3-dimethyl *l*-ascorbic acid monohydrate separated. It had m. p. 58°, $[\alpha]_D^{16°}$ + 30° in water (*c*, 0·8), and an absorption band at λ2350 A. (ε, 10,000) which disappeared when the solution was made alkaline.

6-Trityl 2 : 3-Dimethyl l-*Ascorbic Acid.*—2 : 3-Dimethyl *l*-ascorbic acid (2·5 g.), prepared by the action of excess of diazomethane on *l*-ascorbic acid, was dissolved in pyridine (8 c.c.) and treated with trityl chloride (1·1 mols.). After being kept for 6—7 days at 20°, the mixture was poured into water. The insoluble syrup, after being triturated with water to remove pyridine, became solid and could be filtered off. It was thoroughly washed with water, dried, and recrystallised from methyl alcohol. Yield, after two recrystallisations, 3·3 g. M. p. 156°; $[\alpha]_D$ + 35° in chloroform (*c*, 1·0) (Found : C, 72·1; H, 6·4; OMe, 14·0. Calc. for $C_{27}H_{26}O_6$: C, 72·5; H, 5·9; OMe, 13·9%).

Examination of the mother-liquors revealed the presence of a small quantity of another crystalline substance, which had m. p. 178° after recrystallisation from methyl alcohol and $[\alpha]_D$ + 31° in chloroform (*c*, 0·8). It gave a depression of m. p. when mixed with the substance, m. p. 156° (Found : C, 72·6; H, 6·1; OMe, 13·9. Calc. for $C_{27}H_{26}O_6$: C, 72·6; H, 5·9; OMe, 13·9%).

Isomerisation of 6-trityl 2 : 3-dimethyl *l*-ascorbic acid (m. p. 156°) can be effected by boiling it for 5 minutes with a methyl-alcoholic solution of sodium hydroxide, potassium hydroxide, or sodium methoxide (3·5 mols.) (compare Micheel, *loc. cit.*). The solution is then nearly neutralised with methyl-alcoholic hydrogen chloride and poured into water, and the insoluble white precipitate filtered off. It was washed with water and recrystallised from methyl alcohol. The substance had m. p. 176° and gave no depression when mixed with the compound (m. p. 178°) obtained during tritylation of syrupy dimethyl *l*-ascorbic acid. The best method of bringing about the isomerisation was by dissolving 6-trityl 2 : 3-dimethyl *l*-ascorbic acid in methyl alcohol, followed by saturation with ammonia at room temperature. After 2 days the solution was evaporated and the crystalline isomeride, m. p. 178°, was isolated. It showed $[\alpha]_D$ + 36° in chloroform (*c*, 0·9) (Found : C, 72·7; H, 6·1; OMe, 14·1. Calc. for $C_{27}H_{26}O_6$: C, 72·6; H, 5·9; OMe, 13·9%).

The trityl residue could be removed from the two isomers by dissolving each in 10 parts of chloroform saturated with hydrogen chloride, and keeping the solution for 1 hour at 0° and 1 hour at 15°. The chloroform solution was then exhaustively extracted with water, and the combined aqueous extracts neutralised with silver carbonate, filtered, and evaporated to dryness under reduced pressure. The colourless syrup was extracted with ether; from the cooled ethereal solution, crystalline 2 : 3-dimethyl *l*-ascorbic acid monohydrate separated. It had m. p. 58—59°, $[\alpha]_D^{16°}$ + 30° in water (*c*, 1·0), and an absorption band at λ2350 A. (ε, 10,000).

Methylation of 6-Trityl 2 : 3-Dimethyl l-*Ascorbic Acid with Silver Oxide and Methyl Iodide.*—(a) The substance (m. p. 156°) (0·5 g.) was dissolved in methyl iodide (5 c.c.) and boiled in the presence of excess of silver oxide for 6 hours. The product was isolated by extraction with chloroform and after the chloroform solution had been dried over anhydrous magnesium sulphate the solvent was removed under diminished pressure. When recrystallised from alcohol–ether–light petroleum, the product had m. p. 133°, $[\alpha]_D$ + 31° in chloroform (*c*, 0·5) (Found : C, 73·2; H, 6·1; OMe, 20·2. $C_{28}H_{28}O_6$ requires C, 73·0; H, 6·1; OMe, 20·2%).

(b) The substance (0·2 g.), m. p. 174°, when treated as above gave rise to the same *trityl trimethyl* l-*ascorbic acid*, m. p. 131°, $[\alpha]_D$ + 31·5° in chloroform (*c*, 0·8) (Found : C, 73·4; H, 6·3; OMe, 19·5%). No depression in m. p. was observed when this material was mixed with the product from (a).

Preparation of 2 : 3 : 5-Trimethyl l-*Ascorbic Acid.*—6-Trityl 2 : 3-dimethyl *l*-ascorbic acid (1·3 g.) was dissolved in chloroform (10 c.c.) which had been saturated with hydrogen chloride at − 5°. After being kept for 1 hour at 0° and 1 hour at 15°, the solution was treated with water (20 c.c.), neutralised with silver carbonate, and filtered. The chloroform–water filtrate gave, on evaporation to dryness under diminished pressure at 35°, a crystalline residue containing triphenylcarbinol and *2 : 3 : 5-trimethyl* l-*ascorbic acid*, from which the latter was extracted with water. Removal of the solvent under reduced pressure yielded a syrup (0·56 g.), which readily crystallised. 2 : 3 : 5-Trimethyl *l*-ascorbic acid separated well from ether–light petroleum and had m. p. 69—70°. It was readily soluble in water, alcohol, acetone, less soluble in ether, and insoluble in light petroleum. It did not reduce boiling Fehling's solution. In aqueous solution it showed selective absorption at λ2350 A. (ε, 11,200). The absorption disappeared on addition of alkali. $[\alpha]_D$ − 11·4° in water (*c*, 2·0) (Found : C, 49·3; H, 6·5; OMe, 42·7. $C_9H_{14}O_6$ requires C, 49·5; H, 6·5; OMe, 42·7%).

On treatment with *p*-nitrobenzoyl chloride in pyridine solution a ***mono-p-nitrobenzoate*** was obtained. This was recrystallised from aqueous alcohol and separated in needles, m. p. 118°. It was also obtained as plates, m. p. 103°, which subsequently solidified and remelted at 118°. A mixture of the two modifications had m. p. 118°. The substance showed no appreciable rotation in chloroform (*c*, 0·8) (Found: C, 52·6; H, 4·7; OMe, 24·2; N, 3·9. $C_{16}H_{17}O_9N$ requires C, 52·3; H, 4·7; OMe, 25·3; N, 3·82%).

iso*Trimethyl* l-*Ascorbic Acid*.—2 : 3 : 5-Trimethyl *l*-ascorbic acid (1 g.) in water (20 c.c.) was treated with a solution of 0·3*N*-barium hydroxide (20 c.c.). The specific rotation immediately changed from − 12° to − 47° and no further alteration in rotation occurred on warming for 30 minutes at 40°. The alkaline solution now showed no selective absorption in the ultra-violet. To the solution was then added a slight deficiency of 0·1*N*-sulphuric acid (59 c.c.) and after removal of barium sulphate the solvent was distilled under diminished pressure. The dry syrupy residue was taken up in ethyl alcohol, and excess of ether added. The small quantity of barium salt was filtered off, and the solution evaporated to dryness. The *isotrimethyl ascorbic acid* was a colourless, non-reducing, neutral syrup which had $[\alpha]_D^{15°}$ − 30° in methyl alcohol (*c*, 1·7) and showed no selective absorption in the ultra-violet (tested at 20 mg. %). The substance was distilled in a high vacuum, giving a colourless syrup, b. p. 115° (bath temp.)/0·01 mm., $n_D^{16°}$ 1·4655, which crystallised on keeping. After recrystallisation from ether–light petroleum the acid had m. p. 38°, $[\alpha]_D^{15°}$ − 34·8° in water (*c*, 2·3), and showed no selective absorption in the ultra-violet (tested at 20 mg. %). It was neutral and did not reduce Fehling's solution (Found: C, 49·4; H, 6·1; OMe, 42·3. $C_9H_{14}O_6$ requires C, 49·5; H, 6·5; OMe, 42·7%). When treated with methyl-alcoholic ammonia at 0° for 24 hours, the *iso*trimethyl ascorbic acid readily gave an *amide*, which could be crystallised from acetone; m. p. 115°, $[\alpha]_D^{16°}$ − 35·4° in methyl alcohol (*c*, 1·4), $[\alpha]_D$ − 39° in water (*c*, 1·3). It showed no selective absorption in water or methyl alcohol if examined immediately, but when a methyl-alcoholic solution of the amide was kept at 15° mutarotation took place and a band at λ2350 A. slowly made its appearance, showing that the ascorbic acid ring had been re-formed. In aqueous solution, however, the amide is quite stable, since no absorption band appears and the crystalline substance can be recovered unchanged by evaporation of the solvent under diminished pressure at 15°; m. p. 115° (Found: C, 45·7; H, 7·2; OMe, 38·0; N, 6·0. $C_9H_{17}O_6N$ requires C, 46·0; H, 7·3; OMe, 39·6; N, 5·96%).

Treatment of iso*Trimethyl* l-*Ascorbic Acid with Methyl-alcoholic Hydrogen Chloride*.—On boiling the *iso*trimethyl ascorbic acid (0·5 g.) with methyl-alcoholic hydrogen chloride (50 c.c. of 3%) the specific rotation changed from − 32° to + 3° (constant value) in 20 hours and an absorption band at λ2500 A. (ε, 7000) which had slowly been making its appearance reached a maximum. In alkaline solution this absorption moved to λ2600 A. (ε, 10,000). The acid methyl-alcoholic solution gave no colour with ferric chloride, but after neutralisation of the mineral acid a distinct red colour could be obtained. The removal of the methyl group on C_3 with the re-formation of an ascorbic acid ring had therefore been effected. The solution was neutralised with silver carbonate, filtered, and divided into two portions, A and B.

Portion A gave after removal of solvent a syrup which had properties similar to those of 2-methyl *l*-ascorbic acid. Thus, it was acidic in nature, reduced boiling Fehling's solution, gave a red colour with ferric chloride, and had an absorption band at λ2500 A. which moved to λ2600 A. on addition of alkali. It had $[\alpha]_D^{15°}$ + 2·6° in water (*c*, 2·1) (Found: OMe, 34·0%). This high methoxyl value is probably due to the fact that the solution after refluxing with acid methyl alcohol still contains some unchanged *iso*trimethyl ascorbic acid. On methylation with diazomethane it yielded 2 : 3 : 5-trimethyl *l*-ascorbic acid; this displayed selective absorption at λ2350 A. (ε, 5500) which disappeared on the addition of alkali (Found: OMe, 40·0%).

Portion B was treated with excess of diazomethane and then evaporated under diminished pressure to a syrup. The latter was neutral, did not reduce Fehling's solution, and had $[\alpha]_D$ − 5° in water (*c*, 2·0). In aqueous solution it showed an absorption band at λ2350 A. (ε, 6600), which disappeared on addition of sodium hydroxide (Found: OMe, 41·0%). Portion B therefore consisted mainly of 2 : 3 : 5-trimethyl *l*-ascorbic acid. The syrup was extracted with boiling ether and kept at − 5° for 12 hours; crystalline 2 : 3 : 5-trimethyl *l*-ascorbic acid was then deposited. It had m. p. 68° and an absorption band at λ2320 A. (ε, 11,000).

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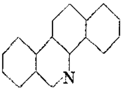
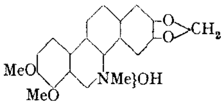
171. *Synthetical Experiments in the Chelidonine–Sanguinarine Group of the Alkaloids. Part I.*

By T. Richardson, Robert Robinson, and E. Seijo.

According to Bruchhausen and Bersch (*Ber.*, 1930, **63**, 2520) and Späth and Kuffner (*Ber.*, 1931, **64**, 370), chelidonine, sanguinarine, and chelerythrine are derivatives of α-naphthaphenanthridine (1 : 2-benzphenanthridine) (I); for example, chelerythrine is represented by the expression (II).

After trial of alternative methods, a general scheme for the synthesis of bases of chelerythrine–sanguinarine type has been worked out and the present communication deals with the preliminaries.

(I.) 

 (II.)

With the co-operation of Dr. M. Liguori, we attempted to apply the phenylnaphthylenediamine synthesis of Atkinson and Thorpe (J., 1906, **89**, 1906) to the piperonyl and veratryl series, but without success.

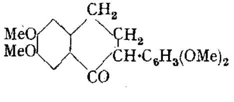
Piperonylacetonitrile, when treated with alcoholic sodium ethoxide, afforded the dimeride, β-*imino-α-cyano-αγ-dipiperonylpropane*, $CH_2O_2{:}C_6H_3{\cdot}CH_2{\cdot}C({:}NH){\cdot}CH(CN){\cdot}C_6H_3{:}O_2CH_2$ (III), in about 50% yield and a by-product was probably 6-*amino*-5-*piperonyl*-2 : 4-*dihomopiperonylpyrimidine*. The imine was readily hydrolysed to β-*keto-α-cyano-αγ-dipiperonylpropane*, but neither the imine nor the keto-nitrile could be converted into a naphthalene derivative. These reactions were also examined in the veratryl series.

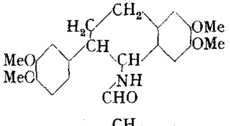
In order to test the applicability of a method similar to Pschorr's phenanthrene synthesis to the phenanthridine group, we reduced the Schiff *base* from 6-nitropiperonal and α-naphthylamine. The diazotisation of the resulting *amine* yielded only a brown tar.

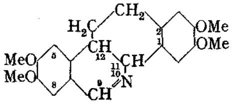
Eventually the following transformations could be effected and a slight modification of them should facilitate the syntheses of chelerythrine and sanguinarine. Condensation of veratraldehyde and acetoveratrone in the usual manner afforded 3 : 4 : 3′ : 4′-*tetramethoxychalkone* and hydrogen cyanide could be added to the double bond with formation of γ-*keto-α-cyano-αγ-diveratrylpropane*, $C_6H_3(OMe)_2{\cdot}CH(CN){\cdot}CH_2{\cdot}CO{\cdot}C_6H_3(OMe)_2$ (IV). The nitrile was then hydrolysed by way of the *amide* to the corresponding *keto-acid*, which was reduced by Clemmensen's method to *αγ-diveratrylbutyric acid*,

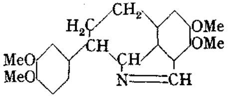
$$C_6H_3(OMe)_2{\cdot}CH(CO_2H){\cdot}CH_2{\cdot}CH_2{\cdot}C_6H_3(OMe)_2$$

(V). The ring-closure of this substance to a tetralone derivative (VI) was best effected by means of phosphoryl chloride and the substituted *formamide* (VII) could be obtained directly from the ketone by interaction with formamide or by way of the *oxime* and related *amine* in the familiar manner.

(VI.) 

 (VII.)

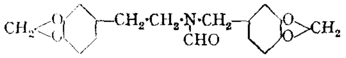
(VIII.) 

 (IX.)

Dehydration of the formamide (VII) by means of phosphoryl chloride yields a base,

$C_{21}H_{23}O_4N$, which might be (VIII) or (IX), but the tetramethoxytetrahydrobenzphenanthridine constitution (VIII) is much the more probable.

A close analogy is provided by the work of Malan and Robinson (J., 1927, 2653), who showed that the action of phosphoryl chloride on formopiperonylmethyl-β-piperonylethylamide (X) gave exclusively a dihydro*iso*quinoline derivative.



(X.)

Some intermediates for a synthesis of chelerythrine along these lines are described.

Experimental.

6-Nitropiperonylidene-α-naphthylamine.—A mixture of 6-nitropiperonal (13·6 g.) and α-naphthylamine (10 g.) was heated (bath at 120—130°) for 2½ hours; the mass had then solidified. The product crystallised from benzene in brownish-yellow prisms (19 g.), m. p. 151—153° (Found: C, 67·6; H, 3·8; N, 8·8. $C_{18}H_{12}O_4N_2$ requires C, 67·5; H, 3·8; N, 8·8%), moderately readily soluble in benzene, dioxan, acetic acid or ethyl acetate.

6-Aminopiperonylidene-α-naphthylamine.—A solution of nitropiperonylidenenaphthylamine (5 g.) in the minimum quantity of hot dioxan was diluted with twice its volume of alcohol, and a hot solution of crystallised sodium sulphide (7·5 g.) in water (20 c.c.) added. After heating on the steam-bath for about 2 minutes, the mixture was added to water (4 vols.) and cooled to 0°. The yellow crystalline substance, after being washed with water, crystallised from alcohol in long yellow needles (3 g.), m. p. 150—151° (Found: N, 9·6. $C_{18}H_{14}O_2N_2$ requires N, 9·7%). The *base* dissolves in dilute hydrochloric acid to a colourless solution, but all attempts to isolate the products of the decomposition of the related diazonium salt were unsuccessful.

Ethyl α-Cyano-β-veratrylacrylate.—The condensation of veratraldehyde and sodium cyanoacetate was effected under the conditions of Lapworth and McRae's method (J., 1922, 121, 1699) and the α-cyano-β-veratrylacrylic acid (m. p. 257—259°), obtained in excellent yield, was esterified by means of boiling 4% methyl-alcoholic hydrogen chloride. The ester, which had m. p. 153—155°, has been previously obtained by Piccinini (*Centr.*, 1904, II, 903) by condensation of veratraldehyde and ethyl cyanoacetate and is stated to melt at 156°.

Veratrylsuccinic Acid.—A mixture of ethyl α-cyano-β-veratrylacrylate (6 g.), alcohol (20 c.c.), and potassium cyanide (3·3 g.) was heated on the steam-bath for 10 minutes, then cooled and acidified with hydrochloric acid. An almost colourless, thick oil separated and after several days this crystallised to a mass of white needles, m. p. 93—95° after recrystallisation from methyl alcohol. The crude product was refluxed during 4 hours with 5 times its weight of concentrated hydrochloric acid and the brownish crystals that separated on cooling were collected and recrystallised from aqueous alcohol, affording colourless needles, m. p. 126—128° (Found: C, 53·0; H, 5·9. $C_{12}H_{14}O_6,H_2O$ requires C, 52·9; H, 5·9%). After keeping in a vacuum desiccator over sulphuric acid the anhydrous acid had m. p. 172—174°. An attempt to condense veratrylsuccinic acid with piperonal, with the help of acetic anhydride and sodium acetate, gave a brown tar, from which only some unchanged substance could be isolated. Veratrylsuccinic acid (7 g.) was esterified by refluxing it with alcohol (25 c.c.) and concentrated sulphuric acid (1 c.c.) for 4 hours. The product was isolated by means of ether and had b. p. 232—235°/15 mm. and did not crystallise at − 10°. The methyl ester was prepared in a similar manner and separated from ether–light petroleum in colourless, minute needles, m. p. 64—66°.

Condensation of Methyl Veratrylsuccinate with Piperonal.—A solution of the methyl ester (3·5 g.) and piperonal (1·9 g.) in ether (10 c.c.) was slowly added to a suspension of alcohol-free sodium ethoxide (1·6 g.) in ether (40 c.c.) cooled in a freezing mixture. The liquid quickly became turbid and after keeping in the ice-box for several hours it was shaken with water (100 c.c.), and the separated aqueous layer acidified. A white substance was deposited and this rapidly became yellow. Crystallisation of the condensation product proved to be difficult, but eventually a crystalline powder was obtained from hot ethyl acetate which, recrystallised from boiling alcohol, afforded long, bright yellow needles, m. p. 127—129° (Found: C, 65·0; H, 4·3. $C_{20}H_{16}O_7$ requires C, 65·2; H, 4·4%). This substance appears to be the *anhydride* of the colourless piperonylideneveratrylsuccinic acid; it is insoluble in alkaline solutions in the cold but dissolves on heating. Acidification then affords the colourless acid, which spontaneously changes into the yellow anhydride. The yield of the crystallised anhydride was poor and for this reason this line of attack was abandoned.

3 : 4 : 3′ : 4′-*Tetramethoxychalkone*.—Aqueous sodium hydroxide (100 c.c. of 10%) was added to a solution of veratraldehyde (100 g.) and acetoveratrone (110 g.) in alcohol (1000 c.c.). After keeping at room temperature for 12 hours with occasional shaking, the yellow crystalline precipitate was collected and recrystallised from boiling alcohol, giving elongated, hexagonal, yellow plates (170 g.), m. p. 116—118° (Found : C, 69·4; H, 6·2. $C_{19}H_{20}O_5$ requires C, 69·5; H, 6·1%).

The *chalkone* is easily soluble in boiling ether, alcohol or acetone. When triturated with concentrated hydrochloric acid, it dissolved to a red solution, from which minute, almost black crystals with a metallic lustre quickly separated. This unstable hydrochloride could not be obtained in an analytically pure condition. The action of hydroxylamine on veratrylideneacetoveratrone affords a *substance* which separates from aqueous alcohol in colourless, slender rosettes of needles, m. p. 152—154° (Found : N, 4·2. $C_{19}H_{21}O_5N$ requires N, 4·1%).

The *phenylhydrazone* or related *pyrazoline* could not be prepared in the usual way, but was obtained by adapting the pyridine method of oximation (Cook, Hewett, and Lawrence, J., 1936, 71). Veratrylideneacetoveratrone (1·5 g.), phenylhydrazine hydrochloride (1·5 g.), and pyridine (5 c.c.) were heated together on the steam-bath for 4 hours. The product crystallised from ethyl acetate in almost colourless, thick prisms, m. p. 159—160° (Found : N, 7·1. $C_{25}H_{26}O_4N_2$ requires N, 6·7%).

α-*Keto-αγ-diveratrylpropane*.—Veratrylideneacetoveratrone (5 g.), dissolved in acetic acid (30 c.c.), was hydrogenated under slight pressure with platinum as catalyst. After 345 c.c. of hydrogen had been absorbed (about 1 hour), no further absorption of the gas occurred, and on dilution of the filtered solution with water, a white crystalline solid was precipitated, which was recrystallised twice from ether and formed colourless needles, m. p. 88—90° (Found : C, 69·2; H, 6·4. $C_{19}H_{22}O_5$ requires C, 69·1; H, 6·7%).

An attempt to prepare the cyanohydrin by means of sodium cyanide and hydrochloric acid in alcoholic solution yielded only a minute amount of needles, m. p. 185—188°, which were not identified, the starting material being for the most part recovered unchanged.

γ-*Keto-α-cyano-αγ-diveratrylpropane* (IV).—The addition of hydrogen cyanide to tetramethoxychalkone could not be accomplished by following the method described in "Organic Syntheses" (1930, X, 80) for the similar reaction of benzylideneacetophenone. After 8 hours, only a small amount of the addition product was formed.

A solution of the chalkone (50 g.) and sodium cyanide (20 g.) in methyl alcohol (250 c.c.) was refluxed, and glacial acetic acid gradually added so that the solution remained faintly alkaline to phenolphthalein. After about 10 minutes a white crystalline mass began to separate. The solution was boiled for a further 10 minutes, cooled, and filtered, and the solid washed well with water. The dried addition product crystallised from acetone in colourless plates (45 g.), m. p. 143—144° (Found : C, 67·6; H, 6·0; N, 3·7. $C_{20}H_{21}O_5N$ requires C, 67·6; H, 5·9; N, 3·9%). The *nitrile* is sparingly soluble in alcohol and ether and easily soluble in hot acetone and acetic acid.

If in the process described above, acetic acid is not added or if boiling is too prolonged, the product is contaminated by another substance consisting of white needles, m. p. 197—199°, probably resulting from the condensation of the nitrile with the unchanged chalkone (cf. Lapworth, J., 1904, **85**, 1358).

The keto-nitrile was recovered unchanged when ring-closure was attempted under the conditions of Hoesch's reaction or with chlorosulphonic acid in chloroform solution. Attempts to protect the carbonyl group by formation of the acetal by means of methyl sulphite (Voss and Blanke, *Annalen*, 1931, **485**, 272) were not successful. The nitrile may be hydrolysed to the acid by boiling concentrated hydrochloric acid, but the product thus obtained is contaminated with an intensely coloured sustance and much material is lost during purification. It is better to proceed by way of the amide.

β-*Veratroyl-α-veratrylpropionamide*.—Concentrated sulphuric acid (10 c.c.) was slowly added to a suspension of the nitrile (10 g.) in glacial acetic acid (100 c.c.). After keeping for 15 minutes at the room temperature, the mixture was poured into ice-water and the white solid was collected and crystallised from alcohol or ethyl acetate; it formed colourless rosettes of needles (9·5 g.), m. p. 160—162° (Found: C, 64·6; H, 6·1; N, 3·8. $C_{20}H_{23}O_6N$ requires C, 64·4; H, 6·2; N, 3·8%).

β-*Veratroyl-α-veratrylpropionic Acid*.—The amide (10 g.) was boiled with aqueous sodium hydroxide (100 c.c. of 7%) and alcohol (50 c.c.) until the evolution of ammonia ceased (5—6 hours). The alkaline solution was diluted with twice its volume of water and kept for ½ hour; when the filtered solution was acidified, the *acid* was precipitated as a white powder, which, crystallised from ethyl acetate–acetic acid, was obtained in pale yellow, slender needles (*ca.* 9 g.), m. p. 193—194° (Found : C, 64·2; H, 5·9. $C_{20}H_{22}O_7$ requires C, 64·2; H, 5·9%).

With phenylhydrazine hydrochloride in pyridine solution this acid furnished pale yellow, stout prisms, m. p. 149—151° (Found : N, 6·6. $C_{26}H_{26}O_5N_2$ requires N, 6·3%). The *derivative* is insoluble in alkaline solutions and is probably the phenylhydrazone anhydride.

αγ-Diveratrylbutyric Acid (V).—The keto-acid (40 g.) was heated with a boiling mixture of toluene (150 c.c.), 5% acetic acid (75 c.c.), concentrated hydrochloric acid (150 c.c.), and amalgamated zinc (100 g.) for 48 hours. Three portions of concentrated hydrochloric acid (50 c.c.) were added at 12-hour intervals. The toluene was separated from the aqueous layer and extracted several times with sodium carbonate solution. Acidification of the extracts gave an oil which rapidly solidified. Crystallised from benzene or aqueous acetic acid, *αγ-diveratrylbutyric acid* was obtained in colourless needles (34 g.), m. p. 118—120° (Found: C, 66·8; H, 6·6. $C_{20}H_{24}O_6$ *requires C, 66·7; H, 6·7%), easily soluble in the common organic solvents except light* petroleum and slightly soluble in hot water.

Dinitro-derivative. Nitric acid (0·5 c.c., *d* 1·4) was added dropwise to a cooled solution of the acid (1 g.) in acetic acid (5 c.c.). After a few minutes the dark red liquid was poured on ice and the precipitated solid was collected, washed with water, and crystallised twice from boiling ethyl acetate, forming pale yellow, thin needles, m. p. 186—188° (Found : N, 6·3. $C_{20}H_{22}O_{10}N_2$ requires N, 6·2%).

1-*Keto*-6 : 7-*dimethoxy*-2-*veratryl*-1 : 2 : 3 : 4-*tetrahydronaphthalene* (VI).—A mixture of αγ-diveratrylbutyric acid (5 g.) and phosphoryl chloride (15 c.c.) was boiled for 4 minutes, cooled, and poured on ice. The white solid which separated was extracted with chloroform, and the extract washed with dilute aqueous sodium hydroxide, dried, and evaporated. The residual oil crystallised from alcohol in colourless plates (3·5 g.), m. p. 147—149° (Found: C, 69·9; H, 6·8. $C_{20}H_{22}O_5$ requires C, 70·2; H, 6·4%).

Oxime. A solution of the ketone (5 g.) and hydroxylamine hydrochloride (5 g.) in pyridine (25 c.c.) was heated at 100° for 5 hours, diluted with water, and extracted with chloroform. The chloroform solution was washed with dilute hydrochloric acid, dried, and evaporated. The *oxime* (4·8 g.) crystallised from alcohol in colourless prisms, m. p. 200—202° (Found : N, 3·8. $C_{20}H_{23}O_5N$ requires N, 3·9%).

1-*Amino*-6 : 7-*dimethoxy*-2-*veratryl*-1 : 2 : 3 : 4-*tetrahydronaphthalene*.—The oxime (4 g.) was dissolved in propyl alcohol (100 c.c.), and sodium (10 g.) added in two portions. When all the sodium had dissolved, water (100 c.c.) was added, the solution neutralised with acetic acid, and the alcohol distilled in steam; the residual oil, on cooling and shaking, slowly solidified to a mass of white needles. These were collected and extracted twice with cold dilute hydrochloric acid. The insoluble residue (2 g.) was unchanged oxime. The acid solution, on basification, afforded a white, amorphous solid, which was dissolved in a mixture of 2*N*-hydrochloric acid and alcohol (1 : 1), and excess of aqueous ammonia added. After several days, colourless silky needles separated, m. p. 119—121° (Found: C, 69·6; H, 7·5; N, 4·1. $C_{20}H_{25}O_4N$ requires C, 69·9; H, 7·3; N, 4·1%).

1-*Formamido*-6 : 7-*dimethoxy*-2-*veratryl*-1 : 2 : 3 : 4-*tetrahydronaphthalene* (VII).—(a) The above amine (0·5 g.) was dissolved in ether (20 c.c.) and mixed with the calculated amount of anhydrous formic acid; the formate then separated as a white crystalline mass. The ether was removed by filtration, and the formate heated at 150° for 5 minutes. The formyl derivative solidified on cooling and was crystallised from methyl alcohol.

(b) 1-Keto-6 : 7-dimethoxy-2-veratryl-1 : 2 : 3 : 4-tetrahydronaphthalene (4 g.) was mixed with formamide (20 c.c.) and gently heated on a sand-bath for 4 days. The solution was cooled, diluted with water, and extracted with chloroform, the extract washed with water and dried, and the solvent removed. The residual oil readily solidified on trituration with methyl alcohol to yield a white crystalline solid (2·5 g.).

The *formyl* derivative prepared by the two methods described crystallised from methyl alcohol, containing a small amount of chloroform, in very fine, matted needles, m. p. 202—203° (Found: C, 68·1; H, 6·9; N, 3·9. $C_{21}H_{25}O_5N$ requires C, 67·8; H, 6·7; N, 3·9%).

6 : 7 : 4′ : 5′-*Tetramethoxy*-3 : 4 : 11 : 12-*tetrahydro*-1 : 2-*benzphenanthridine* (VIII).—A mixture of the formyl derivative (1 g.), toluene (6 c.c.), and phosphoryl chloride (2 c.c.) was boiled for ½ hour. The yellow solid which separated was removed, washed with hot toluene, and suspended in hot methyl alcohol (10 c.c.). The alcohol was made alkaline with ammonia, and the white crystalline solid (0·6 g.) which separated on cooling was collected and recrystallised from methyl alcohol–chloroform (4 : 1); *it formed colourless prisms, m. p. 230—231° (Found:* C, 71·4; H, 6·6. $C_{21}H_{23}O_4N$ requires C, 71·6; H, 6·5%). The reduction and dehydrogenation of this *base* have been accomplished and will be described in a later communication.

Acetopiperone.—Acetopiperone has been previously prepared by oxidising the secondary

alcohol, obtained by interaction of piperonal with methylmagnesium iodide (Klages, *Ber.*, 1903, **36**, 3595; Mameli, *Gazzetta*, 1904, **34**, i, 363), with potassium dichromate or potassium permanganate, but the experimental conditions have not been specified. In our experience potassium permanganate gives the better results.

Potassium permanganate (67 g.) was added in small portions with mechanical stirring to methylpiperonylcarbinol (90 g.), dissolved in acetone (350 c.c.); the temperature was kept at 30—40° by cooling when necessary. Oxidation was complete in about 2 hours. Any small excess of permanganate was destroyed by alcohol. After filtration the manganese precipitate was washed thrice with acetone, and the solvent removed from filtrate and washings. The white crystalline residue consisted of nearly pure acetopiperone (75 g.), m. p. 85°.

Veratrylideneacetopiperone.—Veratraldehyde (15 g.) and acetopiperone (14·5 g.) were condensed together in alcoholic solution by means of sodium hydroxide under the conditions described for the preparation of veratrylideneacetoveratrone (p. 837). The *chalkone* crystallised from alcohol in large, bright yellow prisms, m. p. 133—135° (Found: C, 69·1; H, 5·2. $C_{18}H_{16}O_5$ requires C, 69·2; H, 5·1%). It is less readily soluble than the corresponding tetramethoxy-compound and, though it gives a red coloration with concentrated hydrochloric acid, it does not dissolve to an appreciable extent, nor does it form a characteristic hydrochloride.

γ-Keto-α-cyano-α-veratryl-γ-piperonylpropane.—The addition of hydrogen cyanide to the above chalkone was carried out as described for veratrylideneacetoveratrone (yield, 6 g. from 10 g. of the chalkone); when the mother-liquor was boiled with more sodium cyanide (2 g.) and glacial acetic acid (1 c.c.), a further quantity (3 g.) of the *nitrile* was obtained. It crystallised from acetone in colourless plates, m. p. 144—146° (Found: N, 4·1. $C_{19}H_{17}O_5N$ requires N, 4·1%).

α-Veratryl-β-piperonylpropionamide, prepared like the veratryl analogue, formed colourless plates, m. p. 178—180° (Found: N, 4·1. $C_{19}H_{19}O_5N$ requires N, 3·9%).

β-Imino-α-cyano-αγ-dipiperonylpropane (III).—The following experiments were made by Dr. M. Liguori or in collaboration with him.

A mixture of piperonylacetonitrile (20 g.) and alcoholic sodium ethoxide (1·44 g. of sodium in 30 c.c. of alcohol) was heated for 45 minutes on the steam-bath. The liquid was mixed with water and the oil which then separated was extracted with ether. After removal of the solvent the oily residue was dissolved in alcohol (20 c.c.), ether (30 c.c.) added, and the solution was left to crystallise. After 24 hours the crystals were collected and dried (7·8 g., m. p. 110—111°). The substance separated from alcohol in colourless prisms, m. p. 113—114° (Found: C, 67·3; H, 4·2; N, 8·9. $C_{18}H_{14}O_4N_2$ requires C, 67·1; H, 4·4; N, 8·7%).

From the alcohol–ether mother-liquor there slowly separated another compound, which was collected after 15 days and dried (1·5 g., m. p. 164—165°). The alcohol–ether mother-liquor from this was evaporated, and the residue distilled, nearly all at 130—135°/1 mm. (6·5 g.). Recrystallised from alcohol, the product melted at 44—45°, alone or mixed with piperonylacetonitrile.

The compound of m. p. 164—165° crystallised from alcohol–benzene in clusters of prisms, m. p. 170—171° (Found: C, 66·5; H, 4·1; N, 8·4. $C_{27}H_{21}O_6N_3$ requires C, 67·1; H, 4·4; N, 8·7%). This substance is analogous to cyanbenzyline from phenylacetonitrile and is named in the introduction.

When the reaction mixture was heated for 30 minutes only on the steam-bath, the yield (from 20 g. of nitrile) was 9·5 g. of crude β-imino-α-cyano-αγ-dipiperonylpropane, m. p. 109—110°, and 7·5 g. of recovered nitrile.

β-Keto-α-cyano-αγ-dipiperonylpropane.—A mixture of β-imino-α-cyano-αγ-dipiperonylpropane (5 g.), alcohol (50 c.c.), and 2*N*-sulphuric acid (50 c.c.) was heated for ½ hour on the steam-bath. The reaction mixture was poured into water and the product was isolated by means of ether, dissolved in alcohol, and, after partial evaporation of the solvent, left to crystallise for 2 days; it was then collected (4·7 g., m. p. 121—122°). Recrystallised from alcohol, the *keto-nitrile* had m. p. 122—123° (Found: C, 66·7; H, 4·1; N, 4·2. $C_{18}H_{13}O_5N$ requires C, 66·7; H, 4·0; N, 4·3%).

The *oxime*, prepared from the keto-nitrile and a slight excess of hydroxylamine in alcoholic solution, was twice crystallised and had m. p. 150—151° (Found: C, 64·1; H, 4·3; N, 8·1. $C_{18}H_{14}O_5N_2$ requires C, 63·1; H, 4·1; N, 8·3%).

Attempted ring-closure of ketocyanodipiperonylpropane by means of concentrated sulphuric acid, and by chlorosulphonic acid in chloroform solution, gave unsatisfactory results.

Action of Hydrogen Chloride in Acetic Acid Solution on β-Keto-α-cyano-αγ-dipiperonylpropane and β-Imino-α-cyano-αγ-dipiperonylpropane.—A solution of β-keto-α-cyano-αγ-dipiperonylpro-

pane (3 g., m. p. 122—123°) in glacial acetic acid (60 c.c.) was saturated at 0° with hydrogen chloride. The mixture was kept for 3 days in the ice-chest and then concentrated over sodium hydroxide in a vacuum desiccator. The solid residue was sparingly soluble in cold or boiling water, in dilute mineral acids, and in cold aqueous sodium hydroxide. It was soluble in boiling alcohol, benzene, acetic acid and ethyl acetate. After several recrystallisations from alcohol (charcoal) the product was obtained in thin leaflets, m. p. *ca.* 150° with previous sintering (Found: C, 63·3; H, 4·5; N, 4·1. $C_{18}H_{13}O_5N,H_2O$ requires C, 63·3; H, 4·4; N, 4·1%).

A solution of β-amino-α-cyano-αγ-dipiperonylpropane (1 g., m. p. 113—114°) in glacial acetic acid (10 c.c.) was saturated at 0° with dry hydrogen chloride. After 3 days in the ice chest, the clear solution was evaporated in a vacuum over sodium hydroxide. The solid residue after several crystallisations from alcohol (charcoal) was obtained in thin leaflets, m. p. *ca.* 150° with previous sintering (Found: C, 63·2; H, 4·6; N, 4·3%).

A mixture of the two compounds obtained as above from the imino- and the keto-nitrile behaved like either separately on heating.

A solution of the product of m. p. *ca.* 150° in acetic acid, when mixed with sodium acetate and a solution of *p*-nitrobenzenediazonium chloride, gave no noteworthy coloration.

The substance (0·1 g.) was refluxed with aqueous sodium hydroxide (10 c.c. of 10%) for 2 hours. After cooling, the solution was acidified with hydrochloric acid, the crystalline product which separated was extracted with ether, and the solvent evaporated; the residue (0·07 g.), crystallised from benzene in colourless elongated prisms, m. p. 126—127° (Found: C, 60·2; H, 4·7. Calc. for $C_9H_8O_4$: C, 60·0; H, 4·4%). The hydrolytic product is therefore homopiperonylic acid.

β-Imino-α-cyano-αγ-diveratrylpropane.—A mixture of veratrylacetonitrile (10 g.) and alcoholic sodium ethoxide (0·65 g. of sodium in 10 c.c. of alcohol) was heated for ½ hour on the steam-bath. The reaction mixture was worked up as in the previous case and gave a product (6 g.), m. p. 128—140°, which was a mixture. The crude product (2 g.) was dissolved in alcohol (20 c.c.) and kept at room temperature. After 2 days the separated crystals were collected (1·2 g. of m. p. 130—132°) and recrystallised from alcohol, being obtained in colourless prisms, m. p. 132—133° (Found: C, 67·7; H, 6·4; N, 7·8, 7·9. $C_{20}H_{22}O_4N_2$ requires C, 67·8; H, 6·2; N, 7·9%).

The alcoholic mother-liquors were concentrated and the residue was dissolved in ether (30 c.c.) and kept at room temperature. A crystalline compound that separated was collected after 6 hours (0·5 g., m. p. 165—166°). This substance dissolved in dilute mineral acids and was reprecipitated by the addition of alkali. It dissolved in boiling benzene and alcohol and was sparingly soluble in ether. Recrystallised from alcohol–ether, it was obtained in clusters of flat prisms, m. p. 168—168·5° [Found: C, 67·7; H, 6·5; N, 7·9. $(C_{10}H_{11}O_2N)_3$ requires C, 67·8; H, 6·2; N, 7·9%].

The mother-liquor from the crude product, m. p. 128—140°, was evaporated, and the oily residue distilled. It passed over nearly completely at 150°/1 mm. (1·8 g.). Recrystallised from alcohol, the substance melted at 51—52°, alone or mixed with a specimen of veratrylacetonitrile.

Attempts to improve the yield in the dimerisation of veratrylacetonitrile were unsuccessful. When potassium ethoxide was used, the yield was about 25%, but the results were not consistently obtained. The trimeride (pyrimidine derivative) was obtained as the main product if the heating was prolonged.

6-Bromoveratrylacetonitrile.—A solution of bromine (9 g.) in acetic acid (50 c.c.) was added dropwise to veratrylacetonitrile (10 g.), dissolved in glacial acetic acid (30 c.c.). On dilution with water an emulsion was formed, but a crystalline white solid (11·5 g.) soon separated. It crystallised from alcohol in colourless prisms, m. p. 90—92° (Found: Br, 31·3. $C_{10}H_{10}O_2NBr$ requires Br, 31·3%).

Attempts to dimerise this *bromo-nitrile* led to the recovery of some unchanged substance but to no other crystalline product.

Action of Hydrogen Chloride on Veratrylacetonitrile.—A solution of the nitrile (5 g.) in ether (100 c.c.) was saturated at 0° with dry hydrogen chloride, and powdered zinc chloride (5 g.) added. More hydrogen chloride was passed, and the reactants left for 36 hours in the ice-box. The ether was then decanted and the residual solid was decomposed with water, collected, and extracted with boiling alcohol (75 c.c.). The insoluble portion crystallised from boiling acetone in colourless needles, m. p. 213—215°. This substance contained chlorine and gave analytical figures which could not be interpreted (Found: C, 53·0; H, 5·3%).

The alcoholic solution on concentration afforded a small quantity of red needles, m. p. 207—209°. In another experiment dry hydrogen chloride was passed through an ice-cold solution

of the nitrile (5 g.) in ether (100 c.c.) during 4 hours and the solution was kept in the ice-box for 2 days. The crystalline crust was decomposed with water, and on crystallisation of the solid from alcohol a minute amount of colourless prisms, m. p. 140—142°, was obtained and could not be identified.

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Dyson Perrins Laboratory, Oxford University. [*Received, March 25th,* 1937.]

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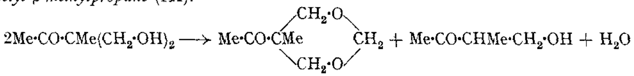
172. *Formaldehyde Condensations with Aliphatic Ketones. Part II. Methyl Ethyl Ketone.*

By Sir Gilbert Morgan and Charles F. Griffith.

Condensation of methyl ethyl ketone with formaldehyde in presence of alkali has previously been shown to give rise to two main products, γ-keto-β-methylbutyl alcohol (I), b. p. 89—90°/11 mm., and γ-keto-β-hydroxymethyl-β-methylbutyl alcohol (II), m. p. 60° * (Morgan and Holmes, J., 1932, 2667). The present communication, which involves a reconsideration of the structure of the benzaldehyde condensation compound of the latter substance, reveals a novel type of reaction in which formaldehyde produced by partial decomposition of (II) condenses with unchanged material to give *αγ-methylenedioxy-β-acetyl-β-methylpropane* (III).



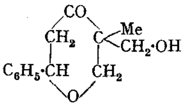
(II.) (III.) (I.)

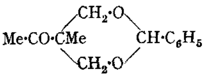
Compound (II) on distillation with potassium hydrogen sulphate yields water, acidic decomposition products, and methyl *iso*propenyl ketone, which on prolonged exposure to light polymerises to a transparent colourless resin as described by Morgan and Holmes (B.P. 404,317). Methyl *iso*propenyl ketone, when condensed with 2 : 4-dinitrophenylhydrazine, gives 1-2′ : 4′-dinitrophenyl-3 : 4-dimethyl-4 : 5-dihydropyrazole identical with that obtained from (I) by Morgan and Holmes (*loc. cit.*). The condensation of (II) with 2 : 4-dinitrophenylhydrazine gives rise to no pyrazole formation, the product being the normal *dinitrophenylhydrazone* (IV), $C_6H_3(NO_2)_2$·NH·N:CMe·CMe$(CH_2·OH)_2$, the constitution of which was established by condensing it with benzaldehyde in the presence of zinc

(V.)

chloride. The condensation product is regarded as *αγ-benzylidenedioxy-β-acetyl-β-methylpropane dinitrophenylhydrazone* (V) for the following reason. Condensation of the parent ketol (II) with benzaldehyde led to a substance described by Morgan and Holmes as 6-phenyl-3-hydroxymethyl-3-methyltetrahydro-γ-pyrone (VI), which, however, has since

(VI.)





(VII.)

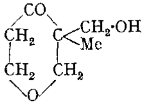
been decomposed by N/100-hydrochloric acid with liberation of benzaldehyde. In view of this reaction the tetrahydro-γ-pyrone structure can no longer be maintained, since

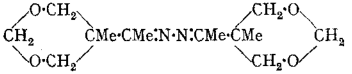
* A melting point of 66° for this substance is cited by Décombe (*Compt. rend.*, 1936, **203**, 1079). Repeated crystallisation from anhydrous benzene has only raised our melting point to 61·5°.

liberation of benzaldehyde would then necessitate rupture of a carbon–carbon linkage, an unlikely occurrence under such comparatively mild conditions (compare Kharasch and Porsche, hydrolysis of phenyldi-1-β-hydroxynaphthylmethane; *J. Org. Chem.*, **1936**, **1**, 266). Furthermore it has not been found possible to acetylate or benzoylate the benzaldehyde compound or to obtain its phenyl- or *p*-xenyl-carbamate, even although structure (VI) includes a free hydroxyl group. Accordingly the substance is now regarded as being αγ-benzylidenedioxy-β-acetyl-β-methylpropane (VII).

The condensation of benzaldehyde with phloroglucinol under acidic conditions has been utilised in confirming the constitution of (VII).* The *benzylidenephloroglucide* is an amorphous substance charring above 300° and changing colour from pink to yellow-brown on drying at 130° (cf. Liebermann and Lindebaum, *Ber.*, 1904, **37**, 1179). It has now been found that 1 mol. (106 g.) of benzaldehyde yields 196 g. of condensation product, which is the same amount as that obtained on hydrolysing 1 mol. (220 g.) of αγ-benzylidenedioxy-β-acetyl-β-methylpropane with hydrochloric acid in presence of phloroglucinol.

Compound (II) on heating with iodine yields methyl *iso*propenyl ketone, water, and a ketone $C_7H_{12}O_3$, boiling at 109°/29 mm., which could neither be acetylated, benzoylated, nor hydrogenated at 150° and under 150 atmospheres' pressure with a platinum catalyst. Its molecular refraction (35·69) corresponded closely with that required for αγ-methylenedioxy-β-acetyl-β-methylpropane (III) (35·43), thus precluding the isomeric tetrahydro-γ-pyrone type of structure (VIII), which still contains one hydroxyl group. Further confirmation of these views was supplied by hydrolysis of (III) with dilute hydrochloric

(VIII.) 

 (IX.)

acid in presence of phloroglucinol (Clowes, *Ber.*, 1899, **32**, 2841). Estimation of the methylene group as formaldehyde-phloroglucide indicated 98·3% hydrolysis, the other product being (II), which was recovered as its 2 : 4-dinitrophenylhydrazone.

The formation of (III) by the action of iodine on the ketol appears to be a new type of reaction and it is reasonable to suppose that under the influence of iodine one molecule of this ketol loses a molecular proportion of formaldehyde to give γ-keto-β-methylbutyl alcohol, which is dehydrated to methyl *iso*propenyl ketone. The free formaldehyde then condenses with a molecular proportion of unchanged ketol (II), to give (III).

To confirm this supposition it was necessary to show that the ketol (II) would in fact condense with formaldehyde under similar conditions to yield (III). This proof was established by comparing the yields of (III) obtained by distilling the ketol with 1% of iodine both alone and with one molecular proportion of formaldehyde. In the first case the yield of (III) was 69·8% of that required by the foregoing theory, whereas in the second case the yield of (III) was 80·7% of that required for the direct condensation of one molecular proportion of (II) with one molecular proportion of formaldehyde. It is apparent, therefore, that the condensation of the ketol with formaldehyde takes place readily in presence of iodine, but it should be noted here that, although potassium hydrogen sulphate has been shown to convert the ketol into methyl *iso*propenyl ketone, it does not catalyse the condensation of ketol with formaldehyde, since (III) was not obtained in this reaction.

The 2 : 4-*dinitrophenylhydrazone* and *semicarbazone* of this new ketone (III) are obtainable, but on attempting to prepare its hydrazone only the *ketazine* (IX) could be isolated.

Experimental.

Distillation of γ-Keto-β-hydroxymethyl-β-methylbutyl Alcohol with Potassium Hydrogen Sulphate.—The ketol (50 g.) was distilled with finely powdered potassium hydrogen sulphate (10 g.). The fraction boiling from 98° to 105°/760 mm. separated into two portions, a top layer

* This method of estimating benzylidene groups is capable of wide application, as, for example, in the case of benzylidene sugar derivatives.

(15·5 g.), which after drying boiled at 96—98°/760 mm. and consisted of methyl *iso*propenyl ketone, b. p. 96—97°, $d_{20^\circ}^{20^\circ}$ 0·8543, $n_D^{20^\circ}$ 1·4224, $[R_L]_D$ 25·00 (calc., 24·81), and a lower aqueous layer (10·5 g.). A second fraction, boiling at 110—120°/760 mm., gave acidic decomposition products and left a tarry residue (28 g.).

1-2′ : 4′-*Dinitrophenyl*-3 : 4-*dimethyl*-4 : 5-*dihydropyrazole*.—Methyl *iso*propenyl ketone (10 g.) was added to a boiling solution of 2 : 4-dinitrophenylhydrazine (23·5 g.) in methyl alcohol (500 c.c.) containing concentrated hydrochloric acid (3 c.c.) and after refluxing for 1½ hours the liquid was cooled at 0° until microscopic orange-red elongated prisms (26 g.) separated, m. p. 190—191°. Admixture with authentic 1-2′ : 4′-dinitrophenyl-3 : 4-dimethyl-4 : 5-dihydropyrazole, m. p. 191°, showed no depression of melting point.

2 : 4-*Dinitrophenylhydrazone of* γ-*Keto*-β-*hydroxymethyl*-β-*methylbutyl Alcohol*.—The ketol (5 g.), m. p. 60—62°, prepared by the method of Morgan and Holmes (*loc. cit.*), was dissolved in methyl alcohol (125 c.c.) and heated with 2 : 4-dinitrophenylhydrazine (7·5 g.) and concentrated hydrochloric acid (2 c.c.) until a homogeneous solution was obtained. On cooling, microscopic orange prisms (7·5 g.) were precipitated, which after recrystallising from ethyl acetate melted at 160—162° (Found : C, 46·8; H, 5·1; N, 18·3. $C_{12}H_{16}O_6N_4$ requires C, 46·15; H, 5·1; N, 17·9%).

αγ-*Benzylidenedioxy*-β-*acetyl*-β-*methylpropane* 2 : 4-*Dinitrophenylhydrazone*.—On addition of light petroleum and water to a well-shaken mixture of the preceding compound (3 g.), benzaldehyde (15 c.c.), and finely powdered dry zinc chloride (5 g.), a yellow precipitate (2·2 g.) was obtained which, when recrystallised from ethyl acetate, separated in minute flattened orange prisms, m. p. 176—177° (Found : C, 57·2; H, 4·8; N, 14·3. $C_{19}H_{20}O_6N_4$ requires C, 57·0; H, 5·0; N, 14·0%).

Condensation of γ-*Keto*-β-*hydroxymethyl*-β-*methylbutyl Alcohol with Benzaldehyde*.—The ketol (20 g.), finely powdered anhydrous zinc chloride (20 g.), and benzaldehyde (50 g.) were shaken together for ½ hour until the mass had solidified (compare Morgan and Holmes, *loc. cit.*). After shaking with water and light petroleum (b. p. 60—80°), a crystalline precipitate (23 g.) was obtained which, when recrystallised from light petroleum, consisted of flattened colourless needles, m. p. 103° alone or mixed with the substance formerly described as 6-phenyl-3-hydroxymethyl-3-methyltetrahydro-γ-pyrone. When the product was warmed with *N*/100-hydrochloric acid, benzaldehyde was evolved readily.

After heating at 100° and cooling to 0°, a solution of this benzaldehyde condensation product (5 g.) in acetic anhydride (3 g.) and pyridine (1 c.c.) gave the unchanged material (4 g.). This failure to acetylate, which would be surprising in the case of a substance containing hydroxyl (VI), is explicable in the case of a substance with the non-hydroxylic structure (VII).

Condensation of Benzaldehyde with Phloroglucinol.—Freshly distilled benzaldehyde (3·587 g.), dissolved in a mixture of 2*N*-hydrochloric acid (20 c.c.) and industrial alcohol (20 c.c.), was refluxed at 100° for 3 hours with phloroglucinol (5·0 g.). Water (100 c.c.) was then added, and the precipitate (6·652 g.) filtered off, washed with water, and dried at 130°. This yellowish-brown amorphous substance was appreciably hygroscopic (Found : C, 72·4; H, 5·1. $C_{13}H_{10}O_3$ requires C, 72·9; H, 4·7%). The amount of *benzylidenephloroglucide* obtainable from redistilled benzaldehyde corresponds with 91·5% of the calculated quantity.

Hydrolysis of αγ-*Benzylidenedioxy*-β-*acetyl*-β-*methylpropane*.—This benzylidene compound (VII) (4·242 g.), dissolved in a mixture of industrial alcohol (20 c.c.) and 2*N*-hydrochloric acid (20 c.c.), was heated at 100° for 3 hours with phloroglucinol (7·0 g.); water (100 c.c.) was then added and the precipitate (3·772 g.) was washed with water (100 c.c.), dried at 130°, and weighed. This amount corresponds with practically complete hydrolysis (99·8%) of the benzylidene compound (VII) on the assumption that benzaldehyde itself gives 91·5% of the insoluble benzylidenephloroglucide, $C_{13}H_{10}O_3$.

The regenerated γ-keto-β-hydroxymethyl-β-methylbutyl alcohol (II) remained in the aqueous-alcoholic filtrate and was characterised by addition to this liquid of 2 : 4-dinitrophenylhydrazine (5 g.) dissolved in hydrochloric acid. When the mixture was left overnight at 0°, a brick-red precipitate (4·5 g.) was obtained; its m. p. and mixed m. p. with the 2 : 4-dinitrophenylhydrazone of γ-keto-β-hydroxymethyl-β-methylbutyl alcohol was 162—163°.

Action of Iodine on γ-*Keto*-β-*hydroxymethyl*-β-*methylbutyl Alcohol*.—The ketol (50 g.) was distilled under atmospheric pressure with iodine (0·5 g.). The distillate from 98° to 108° consisted of two layers, an upper oily layer A (30·5 g.) and a lower aqueous layer B (9 g.), and a tarry residue (6 g.) was left. When fractions A and B were distilled separately, the following products were obtained. *Fraction A* : αγ-methylenedioxy-β-acetyl-β-methylpropane, b. p. 110°/31 mm., 19·0 g.; methyl *iso*propenyl ketone, b. p. 96—97°, 9·0 g.; tarry residue, 0·6 g. *Fraction B* : Water, 7·0 g.; methyl *iso*propenyl ketone, 0·3 g.; tarry residue, 1·2 g.

Action of Iodine and Paraformaldehyde on γ-Keto-β-hydroxymethyl-β-methylbutyl Alcohol.—The ketol (50 g.) was distilled with iodine (0·5 g.) and paraformaldehyde (11·3 g.) under atmospheric pressure. The first fraction, b. p. 98—105°, separated into two layers, a top layer (2 g.) which, after drying, distilled at 120—150°/40 mm. and consisted of unchanged material, and a lower aqueous layer (9 g.). The second fraction (44 g.) distilled at 110—115°/40 mm. and after redistillation was found to consist of *αγ-methylenedioxy-β-acetyl-β-methylpropane*, b. p. 109°/29 mm., $n_D^{20°}$ 1·4495, $d_{20°}^{20°}$ 1·082, $[R_L]_D$ 35·69 (calc., 35·43) (Found: C, 58·5; H, 8·5. $C_7H_{12}O_3$ requires C, 58·3; H, 8·3%).

2 : 4-*Dinitrophenylhydrazone of αγ-Methylenedioxy-β-acetyl-β-methylpropane.*—αγ-Methylenedioxy-β-acetyl-β-methylpropane (5 g.) was refluxed with 2 : 4-dinitrophenylhydrazine (7·5 g.), methyl alcohol (125 c.c.), and concentrated hydrochloric acid (1 c.c.) until a homogeneous solution was obtained. On cooling, orange-yellow rectangular prisms were precipitated which after recrystallising from methyl alcohol melted at 155—157° (Found: C, 48·0; H, 4·9; N, 17·4. $C_{13}H_{16}O_6N_4$ requires C, 48·1; H, 4·9; N, 17·3%).

Semicarbazone of αγ-Methylenedioxy-β-acetyl-β-methylpropane.—A boiling solution of αγ-methylenedioxy-β-acetyl-β-methylpropane (1·8 g.), semicarbazide hydrochloride (1·8 g.), and methyl alcohol (20 c.c.) was saturated with anhydrous potassium carbonate; water (20 c.c.) was added slowly and the solution left overnight at 0°. The white plates (1·4 g.) that had separated were recrystallised from methyl alcohol; m. p. 174—176° (Found: C, 48·6, 48·3; H, 7·7, 7·5; N, 20·1, 19·0. $C_8H_{15}O_3N_3$ requires C, 47·8; H, 7·5; N, 20·9%).

Ketazine of αγ-Methylenedioxy-β-acetyl-β-methylpropane.—Hydrazine sulphate (10 g.) and potassium carbonate (20 g.), dissolved in 50% aqueous methyl alcohol (120 c.c.), were added, with sufficient water (50 c.c.) to bring about complete solution, to αγ-methylenedioxy-β-acetyl-β-methylpropane (10 g.) dissolved in methyl alcohol (50 c.c.). This liquid was refluxed for 2 hours and left for several weeks at 0°. Lemon-yellow needles (2 g.) separated, m. p. 88—90° after recrystallisation from methyl alcohol (Found: C, 59·1; H, 8·8; N, 9·9. The hydrazone $C_7H_{14}O_2N_2$ requires C, 53·1; H, 8·8; N, 17·7%. The *ketazine* $C_{14}H_{24}O_4N_2$ requires C, 59·3; H, 8·4; N, 9·8%).

Hydrolysis of αγ-Methylenedioxy-β-acetyl-β-methylpropane.—The compound (5·0804 g.) was refluxed with 2*N*-hydrochloric acid (200 c.c.) and phloroglucinol (7·00 g.) for 5 hours; a brick-red precipitate of the formaldehyde-phloroglucide $C_7H_6O_3$ was then obtained. After washing with water (500 c.c.) and drying at 130°, this precipitate weighed 4·786 g., whereas complete hydrolysis would yield 4·869 g. of phloroglucide (or 98·3% hydrolysis). To the filtrate from the phloroglucide was added 2 : 4-dinitrophenylhydrazine (9·0 g.), dissolved in 50% hydrochloric acid, and after being left overnight the crystalline precipitate was dried and weighed (5·01 g.); mixed with the 2 : 4-dinitrophenylhydrazone of γ-keto-β-hydroxymethyl-β-methylbutyl alcohol, it gave no depression of melting point (m. p. 160—162°).

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173. *The Condensation of Deoxybenzoin with Aromatic Aldehydes and Ketones. Part II. Condensation of Substituted Deoxybenzoins with Substituted Acetophenones.*

By H. J. Callow and Douglas W. Hill.

Deoxybenzoin condenses with acetophenone in alcoholic potassium hydroxide to form a colourless compound, m. p. 200°, of unknown constitution (Klingemann, *Annalen*, 1893, **275**, 81; Hill, J., 1935, 1115). The reaction is remarkable in that it occurs with the loss only of four hydrogen atoms:

$$2C_{14}H_{12}O + C_8H_8O \xrightarrow{-4H} C_{36}H_{28}O_3$$

An examination of the reaction has now revealed the presence of a second, isomeric, product, m. p. 175°. Condensation also occurs between substituted compounds to give analogous products. 4-Methyl-, 4′-methyl-, 4-methoxy-, 4-chloro-, 4′-chloro-, and 4-bromo-deoxybenzoin reacted similarly with acetophenone (although in the case of the last com-

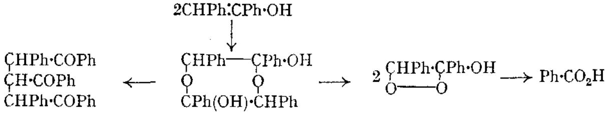
pound the amount available was too small to attempt a fractionation), as did also *p*-methyl-, *p*-methoxy-, *p*-bromo- and *p*-amino-acetophenone with deoxybenzoin.

The features of the reaction were the same in each case. Condensation was always slow (2—6 days) and access to the atmosphere was necessary. In closed flasks, little reaction occurred and in an atmosphere of hydrogen the deoxybenzoin was recovered unchanged. Where condensation occurred, there was a simultaneous formation of benzoic or substituted benzoic acid. It is apparent that the process is one of air oxidation, but that it does not involve the preliminary formation of benzoin was shown by the fact that, when this was substituted for the deoxybenzoin, reaction failed to occur.

The most acceptable explanation of the course of the reaction is the intermediate formation of an unstable oxide. Jenkins (*J. Amer. Chem. Soc.*, 1933, **55**, 1618; 1935, **57**, 2733) has found evidence for peroxide formation in ketones of type (I), which leads on standing in light and air to the formation of an aldehyde and an acid :

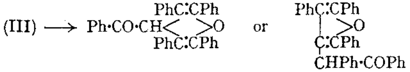
$$\text{(I.)}\quad R'\cdot CH_2\cdot COR \longrightarrow R'\cdot CH{:}C(OH)R \longrightarrow R'\cdot CHO + R\cdot CO_2H$$

If the peroxide formation is preceded by an oxide formation between two molecules of the deoxybenzoin acting in the enol-form (*i.e.*, by half oxidation), an explanation of the reaction with acetophenone offers itself. The necessary enol-form preliminary to the production of the oxide (II) will be predisposed by the presence of the alkali. The oxide, holding its oxygen loosely, will then break down either by reacting with the acetophenone present to give a *phenacylidenedideoxybenzoin* of type (III) or by further oxidation to the peroxide and thence to the acid. Such a phenacylidenedideoxybenzoin would be expected to exist as stereoisomers and in accordance with usage it is proposed to refer to the lower-melting isomer as the *iso*-derivative. Somewhat similar compounds have been obtained by other methods by Knoevenagel and Weissgerber (*Ber.*, 1893, **26**, 436) and by Kostanecki and Tambor (*Ber.*, 1896, **29**, 1495).



(III.) (II.)

The stereochemical relationship of the two isomers was demonstrated in the case of phenacylidenedideoxybenzoin and *iso*phenacylidenedideoxybenzoin by their conversion into the same cyclic derivative. By the action of sulphuric acid or dry hydrogen chloride, in glacial acetic acid both are dehydrated to a compound which may be either 4-benzoyl-2 : 3 : 5 : 6-tetraphenylpyran (IV) or 4-α-phenylphenacyl-2 : 3 : 5-triphenylfuran (V) (cf. Smith, J., 1890, **57**, 645; Dilthey, *J. pr. Chem.*, 1917, **95**, 107).



(IV.) (V.)

In view of the mechanism suggested above, an attempt was made to bring an oxide (dioxan) into reaction with acetophenone under similar conditions. A reaction occurred and the reaction mixture exhibited the characteristic features, but a product could not be isolated.

The *p*-substituted deoxybenzoins were examined in the hope that they would throw further light on the nature of the reaction, since the *p*-substituent will affect, at least, the degree of enolisation. Although the products were formed in differing yields from the various compounds employed, the differences were not such as to be accounted for so readily. The end products are the result of two competitive reactions (oxidation and condensation),

both requiring the same initiation. Since the formation of the acids certainly results from a peroxide intermediate, the lack of regularity in the amount of products may be itself adduced as evidence in favour of the mechanism given. p-Methyl- and p-methoxy-acetophenone behaved like acetophenone, and p-bromoacetophenone gave the greatest yield of condensation product, owing no doubt to the activation of the methyl group. p-Aminoacetophenone, on the other hand, not only decreased the yield of condensation product, but also, apparently, inhibited the further oxidation to acid, since it provided the only case in which unchanged deoxybenzoin was recovered. In all the other cases the conversion either into acid or into condensation product was complete.

Experimental.

Phenacylidenedideoxybenzoin.—A solution of deoxybenzoin (5 g.) and acetophenone (3 g.) in alcohol (50 c.c.) was treated with alcoholic potassium hydroxide (2 g. in 100 c.c.) and kept at room temperature for 1 week; the yellow solution became red and, on scratching, a solid separated. This was filtered off, washed with alcohol, shaken with water to remove potassium benzoate, and crystallised from alcohol. Fractional crystallisation from alcohol yielded *phenacylidenedideoxybenzoin*, which, recrystallised from acetic acid, formed colourless needles, m. p. 199—200° (Found: C, 85·0; H, 5·5. $C_{36}H_{28}O_3$ requires C, 85·4; H, 5·5%). The alcoholic mother-liquors, after concentration, deposited a further quantity of crystals. These were repeatedly crystallised from alcohol and finally from acetic acid, which yielded colourless needles, m. p. 175°, of iso*phenacylidenedideoxybenzoin* (Found: C, 85·5; H, 6·0%).

Phenacylidenedi-(4-methyldeoxybenzoin).—4-Methyldeoxybenzoin and acetophenone in the same quantities and under the same conditions as above gave a solid, which was crystallised from alcohol. The product, alternately crystallised from amyl alcohol and ethyl alcohol, finally separated from the latter in colourless needles, m. p. 238—240° (Found: C, 84·5; H, 6·4. $C_{38}H_{32}O_3$ requires C, 85·0; H, 6·0%). The alcoholic mother-liquor from the first crystallisation was evaporated to one third of its volume, and the resulting solid crystallised several times from alcohol, colourless needles, m. p. 175—176°, of iso*phenacylidenedi-(4-methyldeoxybenzoin)* being obtained (Found: C, 85·4; H, 6·2%). The aqueous washings from the product yielded p-toluic acid on acidification.

Phenacylidenedi-(4′-methyldeoxybenzoin).—4′-Methyldeoxybenzoin (5 g.) and acetophenone (3 g.) were treated as described above and the solid which separated was freed from potassium benzoate and boiled with a large volume of alcohol. The insoluble material crystallised from acetic acid in colourless needles, m. p. 255—256° (Found: C, 84·8; H, 6·4. $C_{38}H_{32}O_3$ requires C, 85·0; H, 6·0%). The alcohol-soluble fraction was crystallised from alcohol many times and obtained in colourless needles, m. p. 240—241°, of iso*phenacylidenedi-(4′-methyldeoxybenzoin)* (Found: C, 84·9; H, 6·4%).

Phenacylidenedi-(4-methoxydeoxybenzoin).—Treatment of 4-methoxydeoxybenzoin (10 g.) and acetophenone (6 g.) as previously described yielded a solid product (0·8 g.), which on fractional crystallisation from alcohol was separated into *phenacylidenedi-(4-methoxydeoxybenzoin)*, colourless needles, m. p. 225° (Found: C, 80·5; H, 5·9. $C_{38}H_{32}O_5$ requires C, 80·3; H, 5·6%), and iso*phenacylidenedi-(4-methoxydeoxybenzoin)*, colourless needles, m. p. 190° (Found: C, 80·8; H, 5·9%). The mother-liquor and aqueous washings, when acidified, yielded anisic acid, m. p. 184°.

Phenacylidenedi-(4-chlorodeoxybenzoin).—The reaction between 4-chlorodeoxybenzoin (5 g.) and acetophenone (3 g.) under the usual conditions was complete after 10 days. The product (2·4 g.) was fractionated from alcohol; the *phenacylidenedi-(4-chlorodeoxybenzoin)* so separated, on further crystallisation from alcohol, formed colourless needles, m. p. 255—256° (Found: C, 74·7; H, 4·5; Cl, 12·1. $C_{36}H_{26}O_3Cl_2$ requires C, 74·9; H, 4·5; Cl, 12·3%). iso*Phenacylidenedi-(4-chlorodeoxybenzoin)*, separated from the reaction product above, on further crystallisation from alcohol was obtained in colourless needles, m. p. 211—212° (Found: C, 74·85; H, 4·45; Cl, 12·2%). p-Chlorobenzoic acid, m. p. 236°, was obtained from the residual reaction mixture and the aqueous washings on acidification.

Phenacylidenedi-(4′-chlorodeoxybenzoin).—4′-Chlorodeoxybenzoin (5 g.) and acetophenone (3 g.) gave 2·3 g. of solid product, which was crystallised many times from alcohol and obtained in colourless needles, m. p. 248° (Found: C, 74·7; H, 4·7; Cl, 12·0. $C_{36}H_{26}O_3Cl_2$ requires C, 74·9; H, 4·5; Cl, 12·3%). The alcoholic mother-liquor yielded, on evaporation, a further crop of crystals. These were recrystallised from alcohol, iso*phenacylidenedi-(4′-chlorodeoxybenzoin)* being obtained in colourless needles, m. p. 234—235° (Found: C, 74·6; H, 4·6; Cl,

12·0%). The reaction mixture and aqueous washings yielded only benzoic acid and unchanged acetophenone.

4-Bromodeoxybenzoin.—Dry *p*-bromobenzamide (10 g.) was added in small portions with stirring to a solution of benzylmagnesium bromide (from 30 g. of benzyl bromide) in dry ether (125 c.c.), the mixture heated and stirred for 48 hours, and the product decomposed with ice-cold dilute sulphuric acid. The solid residue left after steam distillation was crystallised twice from alcohol; p-*bromodeoxybenzoin* separated in colourless needles (3·5 g.), m. p. 115° (Found: C, 61·1; H, 4·1; Br, 28·9. $C_{14}H_{11}OBr$ requires C, 61·1; H, 4·0; Br, 29·1%).

Phenacylidenedi-(4-bromodeoxybenzoin).—4-Bromodeoxybenzoin (2 g.) and acetophenone (1·5 g.), reacting in the usual way, gave a product (0·3 g.), which was washed with water and crystallised twice from alcohol. No attempt was made to fractionate it; m. p. 248° (Found: C, 65·4; H, 4·3. $C_{36}H_{26}O_3Br_2$ requires C, 64·9; H, 4·0%). The aqueous washings yielded *p*-bromobenzoic acid, m. p. 251°, on acidification.

p-*Methylphenacylidenedideoxybenzoin.*—Deoxybenzoin (3 g.) and methylacetophenone (2 g.) in alcohol (30 c.c.) were treated as in previous cases. The product which separated was crystallised first from acetone and finally from alcohol and obtained in colourless needles, m. p. 217° (Found: C, 85·8; H, 6·3. $C_{37}H_{30}O_3$ requires C, 85·1; H, 5·75%). The acetone mother-liquor deposited a second compound, which was crystallised from alcohol many times and obtained in long colourless needles, m. p. 196—197°, of iso-p-*methylphenacylidenedideoxybenzoin* (Found: C, 84·9; H, 5·8%).

iso-p-*Methoxyphenacylidenedideoxybenzoin.*—Deoxybenzoin (3 g.) and *p*-methoxyacetophenone (2 g.) gave after 2 days a solid, which was washed with alcohol and water successively and recrystallised from alcohol, forming colourless needles, m. p. 190—191° (Found: C, 82·4; H, 5·7; OMe, 5·5. $C_{37}H_{30}O_4$ requires C, 82·5; H, 5·6; OMe, 5·75%). The reaction mixture deposited a further quantity of solid on standing, which was treated as before. It crystallised from alcohol in colourless needles, m. p. 209°, of p-*methoxyphenacylidenedideoxybenzoin* (Found: C, 82·5; H, 5·75; OMe, 5·7%).

p-*Bromophenacylidenedideoxybenzoin.*—Deoxybenzoin (5 g.) and *p*-bromoacetophenone (3 g.) were treated with alcoholic potash in the usual manner. The solid which separated from the deep red solution overnight was filtered off and washed with alcohol and water. It was fractionated first from acetone and then from glacial acetic acid. The less soluble fraction was crystallised from alcohol and acetic acid successively and obtained in colourless crystals, m. p. 231° (Found: C, 73·1; H, 4·8; Br, 13·8. $C_{36}H_{27}O_3Br$ requires C, 73·6; H, 4·6; Br, 13·6%). The more soluble fraction crystallised from acetic acid in colourless needles, m. p. 213—215°, of iso-p-*bromophenacylidenedideoxybenzoin* (Found: C, 73·8; H, 4·6; Br, 13·8%).

p-*Aminophenacylidenedideoxybenzoin.*—Deoxybenzoin (5 g.) and *p*-aminoacetophenone (3 g.) were treated as already described. A small quantity of solid that separated after 4 days proved to be potassium benzoate. After further standing, the reaction mixture was treated with water and the small amount of solid product thus obtained was twice crystallised from alcohol. It was purified by alternate crystallisation from benzene and alcohol and obtained in colourless needles, m. p. 205° (Found: C, 82·8; H, 6·0. $C_{36}H_{29}O_3N$ requires C, 82·6; H, 5·6%). The alcoholic mother-liquors yielded deoxybenzoin on concentration.

Dehydration of Isomeric Phenacylidenedideoxybenzoins.—(a) Phenacylidenedideoxybenzoin (0·5 g.), suspended in glacial acetic acid (8 c.c.), was treated with a stream of hydrogen chloride until all the solid had dissolved (5 mins.). The stream was continued for a further 15 minutes, and the solution was kept for 12 hours before being poured into water. The cream-coloured precipitate was crystallised first from dilute alcohol and finally from glacial acetic acid, forming colourless needles, m. p. 118—119° (Found: C, 88·3; H, 5·3. $C_{36}H_{26}O_2$ requires C, 88·2; H, 5·3%).

(b) Phenacylidenedideoxybenzoin (0·5 g.) in glacial acetic acid (20 c.c.) was kept with concentrated sulphuric acid (4 c.c.) for 24 hours. The solution was then poured into water and treated as in (a), yielding the same product.

Treatment of the *iso*-derivative by either of these methods resulted in the formation of the same compound.

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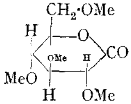
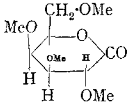
University College, Exeter. [*Received, March 20th, 1937.*]

174. *Optical Rotatory Dispersion in the Carbohydrate Group. Part VIII. Tetramethyl δ-Gluconolactone and Tetramethyl δ-Galactonolactone.*

By T. L. Harris, E. L. Hirst, and C. E. Wood.

In Part IV (*J.*, 1934, 1825) it was shown that the rotatory dispersion of tetramethyl γ-mannonolactone in various solvents could be expressed by a two-term Drude equation, the low-frequency term of which was attributed to induced dissymmetry at the lactonic carbonyl group. When the investigations were extended to the epimeric substance tetramethyl γ-gluconolactone (*J.*, 1935, 295) the dispersion was found to be nearly simple in character, and when attempts were made to derive two-term equations it appeared that a positive term having λ_1^2 *ca.* 0·035 was predominant, and that the comparatively small negative term had λ_2^2 *ca.* 0·075. The former (positive) term corresponds to an active absorption band at λ 1900 A. and can be readily interpreted in terms of induced dissymmetry of the carbonyl group, but the physical meaning of the low-frequency term is still uncertain. We have, therefore, examined other members of the group of lactones which display dispersions not far removed from simplicity. Two such members, specially suitable for accurate measurements on account of high solubilities and rotatory powers, are tetramethyl δ-gluconolactone (I) and tetramethyl δ-galactonolactone (II). These substances possess six-membered ring systems, and we have been able, therefore, to compare the rotatory dispersions of typical δ-lactones with those of γ-lactones containing five-membered ring systems.

(I.) 

 (II.)

The results of the eight series of observations now published show that the rotatory dispersion of both lactones in all the solvents employed can be represented by single-term equations of the Drude–Natanson type:

$$\alpha_\lambda = \frac{k(\lambda^2 - \lambda_0^2)}{(\lambda^2 - \lambda_0^2)^2 + \lambda'^2\lambda^2}$$

Reference to Table I reveals that the values of λ_0^2 are all close to 0·04, corresponding to an active absorption band in the neighbourhood of λ 2000. The carbonyl group of carboxylic acids and esters is known to exhibit absorption bands in this region. The band controlling the rotation of the lactones may, therefore, be ascribed to the lactonic carbonyl group. This implies that the whole of the observed rotation is due to induced dissymmetry and that the partial rotations due to the remaining centres of dissymmetry cancel out amongst themselves, leaving a negligible residual rotation. We have found by further calculations based on the data previously published (*J.*, 1935, 295) that the dispersion of tetramethyl γ-gluconolactone can be expressed by similar single-term equations in which λ_0^2 is approximately 0·04 and λ'^2 *ca.* 0·008. The three lactones are exactly similar in behaviour, and in each case only the term due to induced dissymmetry is observed. These lactones follow the Hudson rotation rule in all solvents, and we have therefore another instance of the connection between rotation rules and induced dissymmetry (see J., 1934, 1826).

The absence of terms occasioned by absorption at shorter wave-lengths (*ca.* λ 1400) is surprising, although a similar case has been encountered amongst the aldehyde-sugars (Hudson, Wolfrom, and Lowry, J., 1933, 1179). On the other hand, in the rotatory dispersion of tetramethyl γ-mannonolactone, the high-frequency term due to the ordinary centres of dissymmetry is prominent, and even predominant under certain conditions. The only structural difference between corresponding mannose and glucose derivatives lies in the configuration of the groups attached to C_2, and in view of the results now disclosed, we intend to examine other lactones in both the mannose and the glucose series in order to determine (*a*) the extent to which the induced dissymmetry is governed severally

by the dissymmetry of C_2 and by that at C_4 (in the γ-lactones: C_5 in the δ-lactones), and (*b*) the types of configuration which render the partial rotation due to induced dissymmetry preponderant in the total observed rotation.

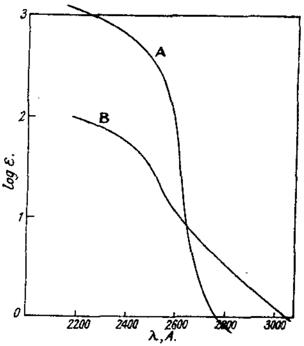
TABLE I.

$$\alpha_\lambda = k(\lambda^2 - \lambda_0^2)/[(\lambda^2 - \lambda_0^2)^2 + \lambda^2\lambda'^2]$$

Tetramethyl δ-gluconolactone.				Tetramethyl δ-galactonolactone.			
Solvent.	k.*	λ_0^2.	λ', A.	Solvent.	k.*	λ_0^2.	λ', A.
$CHCl_3$	34·0	0·0415	760	$CHCl_3$	32·3	0·0456	915
C_6H_6	33·9	0·0429	770	C_6H_6	39·9	0·046	885
Dioxan	35·7	0·0429	845	Dioxan	35·1	0·0415	865
Ether	37·3	0·0388	695	Ether	31·7	0·0412	895

* Calculated for specific rotation values.

The constant λ' in the Drude–Natanson equation gives a measure of the half-width of the active absorption band, and it is apparent from Table I that the values of λ' are large, indicating broad absorption bands. For tetramethyl δ-galactonolactone, the calculated half-width is about 750 A., and for tetramethyl δ-galactonolactone, about 880 A. The corresponding value for tetramethyl γ-gluconolactone is about 900 A. These values are comparable with those (*ca.* 500 A.) measured directly by Hudson, Wolfrom, and Lowry (*loc. cit.*) for the absorption bands of aldehyde-sugar acetates. Moreover, the calculated values of λ' are compatible with the observed absorption spectra of the lactones which display strong general absorption at wave-lengths lower than about 2600 A., without evidence of discrete bands (see fig.).



A. Tetramethyl δ-gluconolactone.
B. Tetramethyl δ-galactonolactone.

It is recognised that the Drude–Natanson equation does not represent with complete accuracy the dispersion phenomena at wave-lengths near the head of the active absorption band (compare *idem, ibid.*), but in the present instances observations which would permit the use of more exact equations are unobtainable because the rotation values, although measurable for wave-lengths on the edge of the absorbing region, are not available for wave-lengths throughout the region of absorption. In these circumstances, the Drude–Natanson equation gives a much closer approximation to the shape of the dispersion curve than does the ordinary Drude equation, which is valid only in regions of complete transparency. We have previously given examples of this (J., 1935, 1658; 1936, 1403) and it has been shown by Sörensen and Trumpy (*Z. physikal. Chem.*, 1935, *B*, **28**, 135) that the dispersions of various sugar acetates, which possess a carbonyl group similar to that of the lactones now under investigation, may be expressed by single-term Drude–Natanson equations having λ_0^2 *ca.* 0·036 and λ' approximately 900 A.

Another feature of the present results requires comment. The induced dissymmetry in the examples now under discussion depends on absorption at λ 2000 approximately, whereas in the case of tetramethyl γ-mannonolactone (when the data were specially favourable for accurate analysis owing to the anomalous dispersion) the induced term depended upon absorption at λ 2500. An intermediate condition is shown by methyl dimethoxysuccinate (Harris, Hirst, and Wood, J., 1935, 1658), the corresponding wave-length being λ 2300. The reason for these divergences is not yet known. Reference to p. 850 shows that the rotations recorded there can be expressed also with considerable accuracy by two-term Drude equations, one term of which is obviously the same in origin as

TABLE II.

In chloroform: c, 14·455; l, 1 dm.; t, 20°; $[\alpha]_D^{20°} + 109·3$; $[\alpha]_\lambda^{20°} = 6·918\alpha_\lambda$.

$$(A)\ \alpha_\lambda = \frac{5·4756}{\lambda^2 - 0·037} - \frac{0·53}{\lambda^2 - 0·064};\quad (B)\ \alpha_\lambda = \frac{4·9345(\lambda^2 - 0·0415)}{(\lambda^2 - 0·0415)^2 + 0·00578\lambda^2}.$$

λ	6708	6292	6104	5893	5805	5515	5225	4887	4548	4252
α	+11·95°	13·73°	14·65°	15·80°	16·33°	18·34°	20·71°	24·08°	28·45°	33·45°
Diff. (A) ...	+0·06	+0·07	+0·05	+0·02	+0·02	+0·05	+0·04	−0·02	−0·08	−0·09
Diff. (B) ...	+0·06	+0·06	+0·03	±0	−0·01	−0·02	±0	−0·07	−0·14	−0·16
λ	4021	3835	3676	3542	3423	3315	3226	3138	3065	
α	+38·45°	43·45°	48·45°	53·45°	58·45°	63·45°	68·45°	73·43°	78·42°	
Diff. (A) ...	−0·04	+0·08	+0·10	+0·17	+0·12	−0·12	+0·04	−0·27	−0·04	
Diff. (B) ...	−0·11	+0·02	+0·06	+0·16	+0·14	−0·07	+0·09	−0·26	−0·16	

In benzene: c, 16·89; l, 1 dm.; t, 20°; $[\alpha]_D^{20°} + 108·9°$; $[\alpha]_\lambda^{20°} = 5·922\alpha_\lambda$.

$$(A)\ \alpha_\lambda = \frac{6·2838}{\lambda^2 - 0·0365} - \frac{0·5138}{\lambda^2 - 0·065};\quad (B)\ \alpha_\lambda = \frac{5·7245(\lambda^2 - 0·0429)}{(\lambda^2 - 0·0429)^2 + 0·0060\lambda^2}.$$

λ	6708	6292	6104	5893	5805	5515	5225
α	+13·89°	15·90°	17·04°	18·39°	18·99°	21·27°	24·08°
Diff. (A)	+0·03	−0·03	+0·01	−0·01	−0·03	−0·06	−0·02
Diff. (B)	+0·05	−0·01	+0·03	±0	−0·03	−0·07	−0·05
λ	4844	4830	4580	4365	4157	4002	3758
α	+28·68°	28·95°	32·95°	36·95°	41·45°	45·45°	53·45°
Diff. (A)	±0	+0·07	+0·23	+0·25	+0·11	+0·03	+0·19
Diff. (B)	−0·07	+0·01	+0·14	+0·12	−0·05	−0·17	−0·06
λ	3649	3542	3433	3345	3265	3193	3108
α	+57·45°	62·45°	67·45°	72·45°	77·45°	82·44°	88·43°
Diff. (A)	−0·03	+0·31	−0·07	+0·06	+0·15	+0·34	+0·13
Diff. (B)	−0·30	+0·03	−0·38	−0·24	−0·15	±0	−0·30

In dioxan: c, 16·44; l, 1 dm.; t, 20°; $[\alpha]_D^{20°} + 114·2°$; $[\alpha]_\lambda^{20°} = 6·083\alpha_\lambda$.

$$(A)\ \alpha_\lambda = \frac{6·646}{\lambda^2 - 0·0378} - \frac{0·756}{\lambda^2 - 0·067};\quad (B)\ \alpha_\lambda = \frac{5·8698(\lambda^2 - 0·0429)}{(\lambda^2 - 0·0429)^2 + 0·00718\lambda^2}.$$

λ	6708	6292	6104	5893	5805	5515	5225
α	+14·18°	16·29°	17·42°	18·78°	19·36°	21·77°	24·49°
Diff. (A)	+0·03	+0·03	+0·08	±0	−0·05	+0·01	−0·09
Diff. (B)	+0·04	+0·03	+0·08	±0	−0·06	±0	−0·11
λ	4887	4681	4545	4376	4179	4028	3896
α	+28·52°	31·55°	33·95°	37·05°	41·45°	45·45°	49·45°
Diff. (A)	−0·14	−0·13	−0·02	−0·12	−0·10	−0·01	+0·06
Diff. (B)	−0·16	−0·15	−0·03	−0·14	−0·10	−0·03	+0·08
λ	3775	3670	3556	3442	3355	3268	3186
α	+53·45°	57·45°	62·45°	67·45°	72·45°	77·45°	82·44°
Diff. (A)	−0·01	+0·03	+0·20	−0·24	+0·14	+0·12	−0·01
Diff. (B)	+0·03	+0·09	+0·28	−0·15	+0·22	+0·11	−0·18

In ether: c, 16·83; l, 1 dm.; t, 20°; $[\alpha]_D^{20°} + 118·9°$; $[\alpha]_\lambda^{20°} = 5·925\alpha_\lambda$.

$$(A)\ \alpha_\lambda = \frac{6·7214}{\lambda^2 - 0·035} - \frac{0·4178}{\lambda^2 - 0·065};\quad (B)\ \alpha_\lambda = \frac{6·2956(\lambda^2 - 0·0388)}{(\lambda^2 - 0·0388)^2 + 0·00479\lambda^2}.$$

λ	6708	6292	6104	5893	5805	5515	5225	4887
α	+15·12°	17·35°	18·54°	20·06°	20·68°	23·23°	26·22°	30·61°
Diff. (A)	+0·01	−0·01	−0·01	+0·02	−0·04	±0	−0·01	+0·04
Diff. (B)	±0	−0·02	−0·02	±0	−0·06	−0·01	−0·03	+0·01
λ	4652	4427	4251	4098	3966	3844	3740	3645
α	+34·45°	38·45°	42·45°	46·45°	50·45°	54·45°	58·45°	62·45°
Diff. (A)	+0·16	−0·11	−0·07	−0·05	+0·02	−0·11	−0·06	−0·08
Diff. (B)	+0·13	−0·13	−0·08	−0·06	+0·02	−0·07	±0	+0·01
λ	3559	3482	3413	3346	3267	3214		
α	+66·45°	70·45°	74·45°	78·45°	83·45°	87·45°		
Diff. (A)	−0·10	−0·06	+0·08	+0·01	−0·24	−0·05		
Diff. (B)	+0·02	+0·10	+0·27	+0·24	+0·02	+0·23		

TABLE III.

In chloroform : c, 15·50; l, 1 dm.; t, 20°; $[\alpha]_D^{20^\circ}$ + 104·4°; $[\alpha]_\lambda^{20^\circ} = 6{\cdot}454\alpha_\lambda$.

$$(A)\ \alpha_\lambda = \frac{7{\cdot}279}{\lambda^2 - 0{\cdot}043} - \frac{2{\cdot}225}{\lambda^2 - 0{\cdot}06};\quad (B)\ \alpha_\lambda = \frac{5{\cdot}0385(\lambda^2 - 0{\cdot}0456)}{(\lambda^2 - 0{\cdot}04556)^2 + 0{\cdot}0084\lambda^2}.$$

λ	6708	6292	5893	5805	5515	5225	4887	4415	4257	4062
α	+12·18°	14·01°	16·17°	16·74°	18·77°	21·19°	24·75°	31·45°	34·45°	38·45°
Diff. (*A*) ...	±0	+0·01	−0·01	+0·01	+0·01	+0·02	+0·02	+0·03	+0·16	−0·02
Diff. (*B*) ...	±0	+0·01	−0·01	+0·01	±0	−0·02	±0	+0·02	+0·14	−0·01

λ	3900	3735	3590	3460	3352	3290	3232	3130	3050
α	+42·45°	47·45°	52·45°	57·45°	62·45°	65·45°	68·45°	73·45°	78·45°
Diff. (*A*) ...	−0·11	+0·01	−0·02	−0·17	±0	±0	+0·06	−0·37	+0·32
Diff. (*B*) ...	−0·06	+0·09	+0·11	−0·03	+0·18	+0·16	+0·14	−0·55	−0·39

In benzene : c, 16·68; l, 1 dm.; t, 20°; $[\alpha]_D^{20^\circ}$ + 129·1°; $[\alpha]_\lambda^{20^\circ} = 5{\cdot}994\alpha_\lambda$.

$$(A)\ \alpha_\lambda = \frac{8{\cdot}7704}{\lambda^2 - 0{\cdot}041} - \frac{2{\cdot}0413}{\lambda^2 - 0{\cdot}06};\quad (B)\ \alpha_\lambda = \frac{6{\cdot}669(\lambda^2 - 0{\cdot}046)}{(\lambda^2 - 0{\cdot}046)^2 + 0{\cdot}00783\lambda^2}.$$

λ	6708	6292	5893	5805	5515	5225	4887	4630	4390	4108
α	+16·16°	18·60°	21·53°	22·23°	24·95°	28·24°	32·87°	37·45°	42·45°	49·95°
Diff. (*A*) ...	−0·05	−0·04	±0	−0·03	−0·02	+0·02	−0·05	+0·08	+0·03	+0·07
Diff. (*B*) ...	±0	+0·01	+0·04	±0	+0·01	+0·04	−0·06	+0·06	−0·02	+0·02

λ	4024	3951	3878	3754	3645	3546	3456	3389	3326
α	+52·45°	54·95°	57·45°	62·45°	67·45°	72·45°	77·45°	81·45°	85·45°
Diff. (*A*) ...	−0·04	−0·01	−0·14	−0·10	±0	+0·01	−0·10	−0·09	−0·20
Diff. (*B*) ...	−0·12	−0·11	−0·19	−0·15	−0·04	+0·05	+0·05	+0·02	−0·03

In dioxan : c, 15·31; l, 1 dm.; t, 20°; $[\alpha]_D^{20^\circ}$ + 111·5°; $[\alpha]_\lambda^{20^\circ} = 6{\cdot}533\alpha_\lambda$.

$$(A)\ \alpha_\lambda = \frac{7{\cdot}126}{\lambda^2 - 0{\cdot}04} - \frac{1{\cdot}749}{\lambda^2 - 0{\cdot}06};\quad (B)\ \alpha_\lambda = \frac{5{\cdot}3764(\lambda^2 - 0{\cdot}0415)}{(\lambda^2 - 0{\cdot}0415)^2 + 0{\cdot}0075\lambda^2}.$$

λ	6708	6292	5893	5805	5515	5225	4887	4640	4450
α	+12·95°	14·81°	17·07°	17·68°	19·81°	22·39°	26·05°	29·45°	32·45°
Diff. (*A*) ...	+0·05	±0	−0·03	±0	−0·01	+0·02	−0·01	+0·06	+0·03
Diff. (*B*) ...	+0·05	+0·01	−0·04	±0	−0·01	+0·02	±0	+0·09	+0·06

λ	4285	4102	3939	3799	3680	3568	3452	3337	3244
α	+35·45°	39·45°	43·45°	47·45°	51·45°	55·45°	60·45°	65·45°	70·45°
Diff. (*A*) ...	+0·01	+0·05	−0·05	−0·12	−0·04	−0·19	±0	−0·37	−0·12
Diff. (*B*) ...	+0·03	+0·12	+0·06	+0·21	+0·12	−0·01	+0·15	−0·27	−0·19

In ether : c, 14·61; l, 1 dm.; t, 20°; $[\alpha]_D^{20^\circ}$ + 100·4°; $[\alpha]_\lambda^{20^\circ} = 6{\cdot}847\alpha_\lambda$.

$$(A)\ \alpha_\lambda = \frac{6{\cdot}217}{\lambda^2 - 0{\cdot}04} - \frac{1{\cdot}60}{\lambda^2 - 0{\cdot}06};\ (B)\quad \alpha_\lambda = \frac{4{\cdot}636(\lambda^2 - 0{\cdot}0412)}{(\lambda^2 - 0{\cdot}0412)^2 + 0{\cdot}0080\lambda^2}.$$

λ	6708	6104	5893	5805	5515	5225	4880	4620	4217
α	+11·06°	13·58°	14·67°	15·12°	16·97°	19·18°	22·43°	25·45°	31·45°
Diff. (*A*) ...	±0	±0	±0	−0·04	−0·01	+0·01	+0·03	+0·03	−0·10
Diff. (*B*) ...	−0·04	−0·04	−0·04	−0·08	−0·05	−0·03	±0	±0	−0·07

λ	4062	3929	3767	3632	3507	3399	3300	3211	3109
α	+34·45°	37·45°	41·45°	45·45°	49·45°	53·45°	57·45°	61·45°	66·45°
Diff. (*A*) ...	−0·04	+0·04	−0·03	+0·06	−0·06	−0·05	−0·10	±0	+0·37
Diff. (*B*) ...	−0·02	+0·08	+0·06	+0·17	+0·05	+0·03	−0·07	−0·15	−0·31

that occurring in the single-term Drude–Natanson equations, but the second has λ_2^2 *ca.* 0·065 and corresponds to absorption at λ 2500. We have previously commented upon the possibility and relative merits of these two methods of representing dispersions which are nearly "simple" (J., 1935, 1659), and we are of the opinion that this second term has no physical significance, and, in particular, is not to be identified with the induced term in the dispersion of tetramethyl γ-mannonolactone. It is probably no more than a numerical correction factor which, over the range of wave-lengths examined, varies fortuitously in the same way as a term of the Drude equation. But with the evidence at present available it is not possible to reject categorically the alternative view, which is nevertheless to be regarded as improbable, that in these lactones the carbonyl group may display two modes of absorption both of which may be capable of giving rise to induced dissymmetry. Further investigations directed towards the elucidation of this point are now being undertaken.

Experimental.

Tetramethyl δ-Gluconolactone.—Tetramethyl glucopyranose was oxidised in the usual way by bromine-water. The product was distilled, and then treated in aqueous solution with a small quantity of potassium permanganate to remove traces of reducing material. The lactone was extracted from the aqueous solution by chloroform, and was finally purified by seven distillations under diminished pressure; $n_D^{15°}$ 1·4561; $[\alpha]_D^{20°}$ + 99° in water (*c*, 0·8). The rotation data are in Table II.

Tetramethyl δ-Galactonolactone.—Specially purified 2 : 3 : 4 : 6-tetramethyl galactose (obtained by hydrolysis of the crystalline anilide) was oxidised by bromine-water (compare Haworth, Ruell, and Westgarth, J., 1924, **125**, 2473). The lactone was then purified and distilled exactly as in the preceding case; $n_D^{15°}$ 1·4602. The relevant data are in Table III.

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175. *Mercuration of O-Trimethylgallaldehyde and Related Substances.*

By Thomas M. Sharp.

In an attempt to increase the yield of 2-nitro-3 : 4 : 5-trimethoxybenzaldehyde (Sharp, J., 1936, 1234), the aldehyde has been mercurated, giving a good yield of 2-*acetoxymercuri*-3 : 4 : 5-*trimethoxybenzaldehyde.* Attempts to replace the acetoxymercuri- by the nitro-group gave mixtures difficult to separate and offering no advantage over the direct nitration process. The method was therefore abandoned, but the mercury compound itself was of interest in being soluble in oils; as oil-solubility is a valuable therapeutic property, some similarly constituted compounds have been mercurated in the hope of obtaining a useful drug. Syringaldehyde, syringic acid, and *O*-trimethylgallic acid were selected for this purpose. All the substances were mercurated readily, but the acetoxymercuri-derivatives were difficult to purify owing to their sparing solubilities and they were, moreover, little soluble in oils. They were purified by conversion into chloromercuri- or bromomercuri-compounds; all these substances have a tendency to lose halogen in solution and this is most pronounced in the case of derivatives of *O*-trimethylgallic acid in alcohols. For example, recrystallisation of 2-bromomercuri-*O*-trimethylgallic acid gives a small amount of the normal salt, but most of the material, of sharp although lower melting point, approximates in composition to a basic salt, $3C_{10}H_{11}O_5HgBr,C_{10}H_{11}O_5HgOH$, and the chloromercuri-derivative has only been obtained as a basic salt, $4C_{10}H_{11}O_5HgCl,C_{10}H_{11}O_5HgOH$. It has not been proved whether these are true basic salts or mixtures of halogenomercuri- and hydroxymercuri-*O*-trimethylgallic acids, but repeated crystallisation failed to make an appreciable difference in the halogen–mercury ratio.

Syringaldehyde was prepared from *O*-trimethylgallaldehyde by partial demethylation with concentrated sulphuric acid at 40°, a method which has been used for the preparation of syringic acid from *O*-trimethylgallic acid (Alimchandani and Meldrum, J., 1920, **117**, 967; Bogert and Coyne, *J. Amer. Chem. Soc.*, 1929, **51**, 571).

The bactericidal action of the mercury compounds has been estimated by Major H. C. Brown, of the Wellcome Bureau of Scientific Research, using the method previously described (Henry, Sharp, and Brown, *Biochem. J.*, 1925, **19**, 515). He found that a 0·1% aqueous solution of 2-bromomercuri-*O*-trimethylgallic acid (as sodium salt) kills *B. typhosus*, Rawlings, in 5 minutes, whereas a 0·01% solution fails to kill. A 0·5% solution of acetoxymercuri-*O*-trimethylgallaldehyde in olive oil kills in 5 minutes, whereas a 0·05% solution fails. 2-Bromomercurisyringaldehyde and 2-chloromercurisyringic acid (as sodium salts) in concentrations of 0·5% and 1% respectively failed to kill the organism.

Experimental.

O-*Trimethylgallaldehyde*.—Molecular proportions of *O*-trimethylgallaldehyde and mercuric acetate in alcohol containing a few drops of acetic acid were boiled under reflux for 4 hours and filtered from mercurous acetate. 2-*Acetoxymercuri*-3 : 4 : 5-*trimethoxybenzaldehyde* slowly separated in soft colourless needles on cooling and more was obtained on concentration of the filtrate. The compound crystallised from alcohol, containing a little acetic acid, in colourless soft needles, m. p. 145—146°.* Yield, 80% of the theoretical (Found: C, 31·7; H, 3·1; Hg, 43·8. $C_{12}H_{14}O_6Hg$ requires C, 31·7; H, 3·1; Hg, 44·1%). It is readily soluble in fatty oils.

O-Trimethylgallic acid (16·96 g.) in alcohol (80 c.c.) was boiled under reflux for 4 hours with mercuric acetate (25·5 g.) in alcohol (160 c.c.) and acetic acid (4 c.c.). The solid which slowly separated was filtered off and a further quantity was obtained by evaporation of the filtrate (yield, 30·8 g.). The solid contained a little mercurous acetate, which was removed by filtration of the solution in sodium hydroxide. When the alkaline solution was poured into excess of 5% hydrobromic acid, 2-*bromomercuri*-3 : 4 : 5-*trimethoxybenzoic acid* was precipitated as a white solid, which after several crystallisations from methyl alcohol formed colourless needles, m. p. 194° (Found: Hg, 41·0; Br, 16·1. $C_{10}H_{11}O_5BrHg$ requires Hg, 40·8; Br, 16·25%). Later crops had m. p. 190° and appeared to be a *basic salt* (Found: Hg, 42·9; Br, 12·6. $C_{10}H_{11}O_5HgOH,3C_{10}H_{11}O_5HgBr$ requires Hg, 42·1; Br, 12·6%). The corresponding *chloromercuri*-compound, obtained by addition of an alkaline solution to hydrochloric acid, crystallised from chloroform or alcohol in colourless needles, m. p. 212°, having the composition of a basic salt (Found: C, 26·6; H, 2·6; Cl, 6·4; Hg, 45·5. $C_{10}H_{11}O_5HgOH,4C_{10}H_{11}O_5HgCl$ requires C, 27·1; H, 2·55; Cl, 6·4; Hg, 45·25%).

Syringaldehyde.—*O*-Trimethylgallaldehyde (5 g.) was added to 25 c.c. of sulphuric acid (*d* 1·84), kept at 40° for 6 hours and left overnight at room temperature. The solution was then poured into cold water (50 c.c.) and extracted with ether, and the aldehyde purified by extraction with sodium bisulphite solution. Yield of pure syringaldehyde, 3 g. It was mercurated by boiling for about 4 hours with an alcoholic solution of mercuric acetate. The acetoxymercuri-compound obtained was contaminated with mercurous acetate and was purified by conversion into 2-*bromomercuri*-4-*hydroxy*-3 : 5-*dimethoxybenzaldehyde* in the usual manner, the solubility in sodium hydroxide solution being due to the phenolic hydroxyl. This salt crystallised from methyl alcohol (in which it was very sparingly soluble) in soft colourless needles, m. p. 260—265° to a cloudy liquid (Found: Hg, 44·1; Br, 17·2. $C_9H_9O_4BrHg$ requires Hg, 43·95; Br, 17·3%).

Syringic Acid.—This was mercurated in the usual way and required about an hour. During the heating a bright yellow solid, presumably a basic salt, separated and was collected; concentration of the filtrate gave a white solid. These were mixed, dissolved in sodium hydroxide solution, filtered from mercurous oxide, and added to excess of hydrochloric acid. The white gelatinous precipitate of 2-*chloromercuri*-4-*hydroxy*-3 : 5-*dimethoxybenzoic acid* was filtered off, washed with water, and crystallised from acetone, from which it was obtained in colourless needles, m. p. 230° (decomp.) (Found: C, 25·1; H, 2·3; Hg, 46·0. $C_9H_9O_5ClHg$ requires C, 24·9; H, 2·1; Hg, 46·3%).

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176. *Morellin, a Constituent of the Seeds of* Garcinia Morella.

By B. Sanjiva Rao.

Garcinia morella belongs to a large genus of evergreen trees of the tropics which yield the gamboge of commerce. From the seeds a semi-solid edible oil is obtained, and the pericarp contains a yellow colouring matter. Extraction of the pericarp with hot alcohol yields, in addition to amorphous substances, a yellow crystalline lævorotatory phenol, m. p. 154°, for which the name *morellin* is suggested. Morellin has the composition $C_{30}H_{34}O_6$, and it contains apparently four hydroxy-groups, since it yields a *tetra-acetate*, m. p. 178—179°. Two of the hydroxy-groups are readily methylated by methyl iodide in acetone solu-

* All m. p.'s are corrected.

tion in the presence of potassium carbonate; the *dimethyl* ether has m. p. 156°, and a *trimethyl* ether, m. p. 172°, can be prepared from its sodio-derivative. Two ethylenic linkages are also present since morellin yields a *dihydrochloride*, m. p. 131°, and a *tetrabromide*, m. p. 138—139°. On treatment with hydroxylamine an amorphous *dioxime* is obtained, which suggests two carbonyl groups, the presence of one of them being confirmed by the preparation of a crystalline *mononitroguanylhydrazone*, m. p. 205·5°.

Morellin is a somewhat unstable substance; it is resinified by prolonged digestion with alcohol or when kept at 100° for some hours. It is also converted into an amorphous substance by solution in alcoholic potassium hydroxide. A crystalline isomeride, iso*morellin*, m. p. 116°, is obtained when an ethereal solution of the phenol is shaken with aqueous potassium hydroxide or when it is digested with acetyl chloride in benzene solution in the presence of potassium carbonate.

On fusion with alkali morellin gives a variety of products, of which the following have been identified: *dl*-methylheptenol, phloroglucinol, acetic, *iso*valeric, methylsuccinic and homophthalic acids. A liquid ditertiary *glycol*, $C_{16}H_{22}O_2$, probably containing two ethylenic linkages and having a strong odour reminiscent of amyl alcohol, is also formed.

Whilst the evidence at present available is insufficient to warrant the assignment of any structure to morellin, it would appear probable that it is related to mangostin, the yellow colouring matter present in the pericarp of the seeds of *Garcinia mangostana*, which has formed the subject of a detailed investigation by Murakami (*Annalen*, 1932, **496**, 122). This phenol, like morellin, is a derivative of phloroglucinol and gives on potash fusion, amongst other products, *dl*-methylheptenol, acetic and *iso*valeric acids.

Experimental.

The dry powdered pericarp of the seeds (100 g.) was digested with alcohol (300 c.c.); the hot filtered solution on standing for some hours depositing morellin (7 g.), m. p. 148—150°. A further quantity (3 g.) of the colouring matter can be obtained by extraction with fresh alcohol (300 c.c.). Addition of water to the filtrate precipitated an amorphous yellow solid (11 g.), which was not further investigated. *Morellin* crystallised from methyl or ethyl alcohol in golden-yellow needles or rhombic prisms, m. p. 154°, $[\alpha]_D$ − 594° (in chloroform, *c* 4·5) [Found: C, 73·3; H, 7·3; *M* (in benzene) 485. $C_{30}H_{34}O_6$ requires C, 73·5; H, 7·0%; *M*, 490]. Morellin is insoluble in water, but readily soluble in most of the ordinary organic solvents with the exception of the alcohols and ligroin. Its alcoholic solution gives with ferric chloride a brownish-green coloration. It is insoluble in sodium carbonate solution, but dissolves in alcoholic potassium hydroxide to give a red potassium salt, which on acidification deposits an amorphous solid, m. p. 73° (Found: C, 62·5; H, 6·7%). iso*Morellin* was obtained when a mixture of morellin (2 g.), acetyl chloride (4 g.), and potassium carbonate (4 g.) in benzene was heated for 4 hours. It crystallised from ethyl alcohol in golden-yellow prisms, m. p. 116°, $[\alpha]_D$ − 561° (in chloroform, *c* 3·9) (Found: C, 73·5; H, 7·5%). Its alcoholic solution gave a dark brown ferric chloride coloration.

Morellin Dihydrochloride.—Although morellin is not affected by digestion with concentrated hydrochloric acid, a *dihydrochloride* is formed when a solution of morellin (2 g.) in acetic acid (15 c.c.) is saturated with hydrogen chloride. Addition of ice precipitates an orange solid, m. p. 131° after crystallisation from methyl alcohol (Found: Cl, 12·3. $C_{30}H_{34}O_6$,2HCl requires Cl, 12·6%).

Morellin Tetrabromide.—To a solution of morellin (2·5 g.) in chloroform (20 c.c.) a solution of bromine (1·74 g.) in chloroform was added. Removal of the solvent in a vacuum gave orange-yellow crystals which, after recrystallisation from alcohol, had m. p. 138—139°, $[\alpha]_D$ − 156° (in chloroform, *c* 4·91) (Found: Br, 39·7. $C_{30}H_{34}O_6Br_4$ requires Br, 39·5%).

Morellin dioxime, prepared by treatment of an alcoholic solution of morellin with hydroxylamine hydrochloride and sodium acetate, was an amorphous yellow powder, m. p. 148—149° (Found: C, 68·8; H, 7·1; N, 5·6. $C_{30}H_{36}O_6N_2$ requires C, 69·2; H, 6·9; N, 5·6%). *Morellin mononitroguanylhydrazone* crystallised from alcohol–ethyl acetate in thick yellow prisms, decomp. 205·5°, $[\alpha]_D$ − 748° (in chloroform, *c* 3·1) (Found: C, 62·4; H, 6·6. $C_{31}H_{37}O_7N_5$ requires C, 62·9; H, 6·3%). *Morellin tetra-acetate*, prepared by digestion of the phenol with acetic anhydride and sodium acetate, crystallised from methyl alcohol in yellow prisms, m. p. 178—179°, $[\alpha]_D$ −327° (in chloroform, *c* 4·7) (Found: C, 69·6; H, 6·4; OAc, 25·8. $C_{38}H_{42}O_{10}$ requires C, 69·3; H, 6·4; 4OAc, 26·1%).

Morellin Dimethyl Ether.—To a boiling solution of morellin (10 g.) in acetone (100 c.c.) containing potassium carbonate (10 g.) in suspension, methyl iodide (20 g.) was added during 8 hours. The filtered solution gave, on removal of the solvent, a solid which crystallised from methyl alcohol in pale yellow rosettes of rectangular prisms, m. p. 156°, $[\alpha]_D - 242°$ (in chloroform, *c* 6·2) [Found : C, 74·0; H, 7·2; OMe, 12·4. $C_{30}H_{32}O_4(OMe)_2$ requires C, 74·1; H, 7·4; OMe, 12·0%]. Its alcoholic solution gave no colour with ferric chloride. The *dioxime* separated from dilute alcohol as a white amorphous powder, m. p. 118°, $[\alpha]_D + 241°$ (in chloroform, *c* 4·0) (Found : N, 4·9. $C_{32}H_{40}O_6N_2$ requires N, 5·1%). The *diacetyl* derivative of the dimethyl ether separated from alcohol as a microcrystalline powder, m. p. 82—83° (Found : C, 69·0; H, 6·8; OAc, 14·2. $C_{36}H_{42}O_8$ requires C, 69·2; H, 6·8; 2OAc, 14·3%), and the *tetrabromide*, prepared in chloroform solution, after crystallisation from methyl alcohol, had m. p. 124° (Found : Br, 38·0. $C_{32}H_{38}O_6Br_4$ requires Br, 38·4%).

Morellin Trimethyl Ether.—The dimethyl ether (5 g.) in toluene (50 c.c.) was heated with sodium wire (0·5 g.) until evolution of hydrogen ceased. The toluene solution was decanted from unchanged sodium and, after the addition of methyl iodide (15 g.), heated for 4 hours. Removal under diminished pressure of the toluene from the filtered solution gave a solid, which separated from benzene–ligroin as a microcrystalline yellow powder, m. p. 170—172° [Found : C, 74·6; H, 7·5; OMe, 17·0. $C_{30}H_{31}O_3(OMe)_3$ requires C, 74·4; H, 7·6; OMe, 17·5%]. The use of methyl sulphate in place of methyl iodide gave a resinous product.

Fusion of Morellin with Potassium Hydroxide.—Morellin (20 g.) with potassium hydroxide (100 g.) and water (10 c.c.) was heated in a nickel crucible at 220° in a current of nitrogen (mechanical stirring), the volatile products of the fusion being collected in a well-cooled receiver. The distillate, which had a strong odour of amyl alcohol, was dissolved in ether, the ethereal extract dried, and the solvent removed. On distillation under diminished pressure two fractions were obtained : (a) b. p. 80—85°/15 mm., $d_{30°}^{30°}$ 0·852, $n_D^{30°}$ 1·4450, identified as *dl*-methylheptenol by oxidation with chromic acid to *dl*-methylheptenone, semicarbazone, m. p. 129—130° (Found : N, 22·8. Calc. for $C_9H_{17}ON_3$: N, 22·9%); and (b) an *oil*, b. p. 130—140°/8 mm., $d_{30}^{30°}$ 0·917, $n_D^{30°}$ 1·47898, which resembled amyl alcohol in odour [Found : C, 76·1; H, 10·9; OH, 12·7; *M* (Rast), 258. $C_{16}H_{26}(OH)_2$ requires C, 76·2; H, 11·1; OH, 13·5%; *M*, 252]. The alcohol did not react with phthalic anhydride at 140°, and titration with bromine showed the presence of two ethylenic linkages.

The fusion was dissolved in water, saturated with carbon dioxide, and extracted with ether. The residue after removal of the ether was distilled in steam, a volatile oil being obtained which resembled thymol in odour and partly crystallised on keeping, m. p. 50—55°. It gave a bluish-black coloration with alcoholic ferric chloride and formed a phenylurethane, m. p. 149—150° (Found : C, 72·8; H, 5·6%), which was not identified. The aqueous residue from the steam distillation was concentrated and extracted with ether, which left on evaporation a solid, m. p. 219°, identified as phloroglucinol by conversion into its trinitro-derivative, m. p. 165°, both alone and in admixture with trinitrophloroglucinol (Found : N, 15·8. Calc. for $C_6H_3O_9N_3$: N, 16·1%).

The sodium carbonate solution from which the phenols had been separated was acidified with sulphuric acid and distilled in steam. The acids volatile in steam were extracted with ether and distilled under diminished pressure, four fractions being obtained : (i) b. p. 85—90°/65 mm., (ii) 95°/35 mm., (iii) 96—98°/35 mm., and (iv) 140—150°/10 mm. Fraction (i) was a mixture of acetic and *iso*valeric acids, characterised by the preparation of acetanilide, m. p. 121°, and *iso*-valeramide, m. p. 135—136°. Fractions (ii) and (iii) were pure *iso*valeric acid, and (iv), which was not identified, appeared to be phenolic.

The aqueous residue from the steam distillation was extracted with ether; this left on evaporation an oil, which partly solidified. The solid after crystallisation from water had m. p. 176° and was identified as homophthalic acid [Found : C, 59·6; H, 5·0; *M* (Rast), 185. Calc. for $C_9H_8O_4$: C, 60·0; H, 4·4%; *M*, 180]. The amide had m. p. 180—181° and the *p*-nitrobenzyl ester, m. p. 135°. The liquid acids remaining after removal of the homophthalic acid were converted through their silver salts into the methyl esters. These, on fractionation, gave an oil, b. p. 88—95°/8 mm., which consisted essentially of methyl methylsuccinate, since it gave an amide, m. p. 224°, and a *diphenacyl* ester, m. p. 101° (Found : C, 69·0; H, 5·8. $C_{21}H_{20}O_6$ requires C, 68·5; H, 5·4%). The higher-boiling fractions contained, in addition to homophthalic acid, two other acids which were not obtained pure.

The author is indebted to Professor J. L. Simonsen, F.R.S., for suggesting this investigation, morellin having first been isolated in his laboratory at Dehra Dun by the late Mr. M. Gopal Rau.

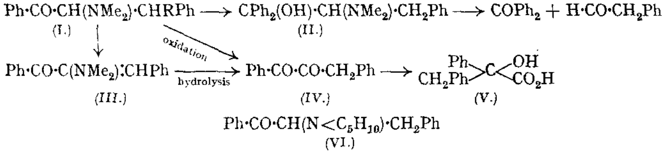
Indian Institute of Science, Bangalore. [*Received, April 20th, 1937.*]

177. *Reactions of α-Amino-ketones.*

By Thomas S. Stevens and B. Arthur Hems.

In establishing the constitutions of substances analogous to (I) it was difficult to prove that the nitrogen atom occupied the α- and not the β-position with respect to the carbonyl group (Stevens, *J.*, 1930, 2109). A feasible procedure is now described, together with some incidental observations.

The *hydroxy-amine* (II), prepared from (I, R = H) by the Grignard reaction, was comparatively stable even to acid permanganate, but it was oxidised very readily by persulphate, or by manganese dioxide and sulphuric acid, to benzophenone and phenylacetaldehyde. This reaction, which establishes the point at issue, was not brought about by other oxidising agents; nor could a similar oxidation of (I) itself be achieved. The nature of the breakdown, and the reagents employed, recall the oxidative fission of narcotine and its analogues, which, like (II), contain the group ·O·CAr·C·NAlk_2. A similar series of reactions was carried out with (I, R = Me) and with (VI), but it failed in the case of (I, R = Ph), probably because the required aldehyde was not volatile enough to be protected from further oxidation.



Air slowly oxidised alkaline solutions of (I), yielding, by a curious dehydrogenation, the unsaturated *base* (III), together with phenylbenzylglycollic (V) and benzoic acids. The constitution of (III) follows from its hydrolysis to phenylbenzylglyoxal (IV) and its synthesis from phenyl bromostyryl ketone and dimethylamine. The acid (V) presumably arose by benzilic transformation of (IV) (compare Widman, *Ber.*, 1916, **49**, 477; Jörlander, *ibid.*, 1917, **50**, 416). Independent experiments showed that (III) was not produced from dimethylamine and (IV), nor (V) from (III) *via* (IV), under the conditions of the dehydrogenation. A similar result could not be achieved by other oxidising agents, and other bases, *e.g.* (I, R = Me), could not be oxidised in an analogous manner.

The allyl radical, and others containing a similarly situated unsaturated centre, are detached from tertiary bases by cyanogen bromide with special facility. From (I, R = H) which contains a *carbonyl* double bond in a position corresponding to that of the olefinic double bond in an allylamine, cyanogen bromide removed on the contrary a methyl group; and in the case of (VI) the usually stable piperidine ring was opened.

Experimental.

2-Dimethylamino-1-hydroxy-1 : 1 : 3-triphenylpropane (II).—The base (I, R = H) was added to excess of phenylmagnesium bromide in ether, the vigorous reaction completed by 1 hour's boiling, and after treatment with ice and ammonium chloride the product (II) was extracted from the ethereal layer by acid; yield, almost quantitative. It crystallised from ligroin or methyl alcohol in small prisms, m. p. 75°, whose solutions in concentrated sulphuric acid changed from orange-red to colourless to bluish-green in a few seconds (Found: N, 4·0. $C_{23}H_{25}ON$ requires N, 4·2%). The *picrate* formed irregular yellow prisms from alcohol, m. p. 188° with previous softening (Found: $C_6H_3O_7N_3$, 41·1. $C_{23}H_{25}ON,C_6H_3O_7N_3$ requires $C_6H_3O_7N_3$, 40·9%). The analogous hydroxy-amines described below were prepared in the same way.

Oxidation. A solution and suspension of the base (II) in 0·05*N*-sulphuric acid (1 equiv.) was distilled with gradual addition of a slight excess of 0·5% ammonium persulphate solution. The ethereal extract of the distillate yielded 10% of phenylacetaldehyde, separated as bisulphite compound and identified as semicarbazone (mixed m. p.), and also much benzophenone, characterised as dinitrophenylhydrazone (mixed m. p.).

2-Dimethylamino-1-hydroxy-1 : 1 : 3-triphenylbutane.—This base, prepared from (I, R = Me) (α-form; Stevens, *loc. cit.*), was a gum. The sparingly soluble *hydrochloride* crystallised from methyl alcohol–ether in stout irregular plates, m. p. 226—231° (decomp.) (Found: HCl, 9·6. $C_{24}H_{27}ON,HCl$ requires HCl, 9·6%). The base was oxidised in the same way as its lower homologue, except that 0·02*N*-sulphuric acid was used, and α-phenylpropaldehyde (prepared for comparison according to Tiffeneau, *Ann. Chim. Phys.*, 1907, **10**, 351) and benzophenone were isolated and identified similarly.

2-Piperidino-1-hydroxy-1 : 1 : 3-triphenylpropane (VI), prepared from ω-piperidino-ω-benzylacetophenone (Stevens, *loc. cit.*), formed prisms from ligroin, m. p. 145—147° (Found: N, 3·8. $C_{26}H_{29}ON$ requires N, 3·8%). The oxidation and the identification of the products were performed as in the previous case.

2-Dimethylamino-1-hydroxy-1 : 1 : 3 : 3-tetraphenylpropane, prepared from (I, R = Ph) (Stevens, *loc. cit.*), and purified through its insoluble sulphate, crystallised from ligroin in warty masses, m. p. 105° (Found: N, 3·5. $C_{29}H_{29}ON$ requires N, 3·4%). Oxidised in the same way as (II), it gave only benzophenone, and neither diphenylacetaldehyde nor diphenylacetic acid could be detected.

ω-Dimethylamino-ω-benzylideneacetophenone (III) was readily prepared by the method of Dufraisse and Moureu (*Bull. Soc. chim.*, 1927, **41**, 469), the piperidine being replaced by 10% ethereal dimethylamine. It crystallised from alcohol in scarlet needles, m. p. 62° [Found: N, 5·4; *M* (Rast), 240. $C_{17}H_{17}ON$ requires N, 5·6%; *M*, 251]. The base (I), in 10 parts of 2·5*N*-alcoholic sodium ethoxide solution, was oxidised by a slow current of pure dry air for 6 hours at 70°. The ethereal extract of the diluted mixture yielded (III) (mixed m. p.) on evaporation. This base gave dimethylamine picrate (mixed m. p.) with alcoholic picric acid, and ethereal oxalic acid (compare Dufraisse and Moureu, *loc. cit.*) converted it into phenylbenzylglyoxal (IV), m. p. 80° (quinoxaline, m. p. and mixed m. p. 98°). The alkaline aqueous-alcoholic liquors from the oxidation gave a mixture of acids resolved by crystallisation from benzene into more soluble benzoic acid (mixed m. p.) and less soluble phenylbenzylglycollic acid (V) (mixed m. p.), which yielded benzophenonedinitrophenylhydrazone (mixed m. p.). When the sodium ethoxide solution was replaced by alcoholic potash, the products were the same, but the yield of the acid (V) was negligible.

Action of Cyanogen Bromide on (I).—The base was refluxed for 30 minutes with cyanogen bromide (1½ mols.) in ether. After removal of ether and cyanogen bromide in a vacuum, the residual *ω-methylcyanoamido-ω-benzylacetophenone* was crystallised from methyl alcohol; m. p. 110° (Found: N, 10·7. $C_{17}H_{16}ON_2$ requires N, 10·6%). By 5 minutes' boiling with 10% sulphuric acid, the cyanoamide was completely converted, without dissolving, into the related *urea*, 226° (Found: N, 10·1. $C_{17}H_{18}O_2N_2$ requires N, 9·9%). On similar treatment, ω-piperidino-ω-benzylacetophenone (VI) yielded *ω-(ε-bromoamylcyanoamido)-ω-benzylacetophenone*, m. p. 83° after crystallisation from methyl alcohol (Found: N, 7·0; Br, 20·7. $C_{21}H_{23}ON_2Br$ requires N, 7·0; Br, 20·1%).

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178. *The Photosynthesis of Hydrogen Chloride in Oxygen-rich Mixtures: The Quantum Efficiency of Water Formation.*

By MOWBRAY RITCHIE.

THE photo-combination of hydrogen and chlorine may be considered in three main divisions: (*a*) oxygen-free mixtures, (*b*) oxygen-rich mixtures characterised by direct proportionality between rate of reaction and intensity of absorbed light, and (*c*) the "transition region," in which the characteristics of both (*a*) and (*b*) can be related to the amount of oxygen present. In the region (*b*), provided the ratio of chlorine to hydrogen concentrations is not too large, the retarding effect of oxygen is undoubtedly to be ascribed mainly to the removal of the hydrogen atoms of the reaction chains (Norrish and Ritchie, *Proc. Roy. Soc.*, 1933, *A*, **140**, 713; Norrish, *Trans. Faraday Soc.*, 1931, **27**, 461; Krauskopf and Rollefson, *J. Amer.*

Chem. Soc., 1934, **56**, 327), and in this connection Norrish and Ritchie (*loc. cit.*) considered as most probable the following mechanism:

$$H + O_2 + H_2 = H_2O + OH$$
$$H + O_2 + HCl = H_2O + ClO$$
$$H + O_2 = HO_2$$

The last equation was taken to represent a straight bimolecular reaction (cf. Bates and Lavin, *J. Amer. Chem. Soc.*, 1933, **55**, 81); the rate of hydrogen chloride formation would on this account be independent of the addition of a foreign gas such as nitrogen. On the other hand, Bodenstein and Schenk (*Z. physikal. Chem.*, 1933, *B*, **20**, 420), from a comprehensive study of the quantum efficiencies of both hydrogen chloride and water formation, proposed the scheme

$$H + O_2 + M = HO_2 + M \qquad HO_2 + Cl_2 = HCl + ClO_2$$
$$HO_2 + H_2 = H_2O + OH \qquad HO_2 + HCl = H_2O + ClO$$

The key reaction is here the stabilisation of the HO_2 complex by a third gas molecule. Nitrogen acting in this capacity would facilitate the removal of hydrogen atoms and thus produce a decrease in the rate of hydrogen chloride photosynthesis. The question is of importance in more than one connection: any system in which hydrogen atoms are produced in an atmosphere of oxygen and hydrogen (*e.g.*, the mercury-sensitised formation of hydrogen peroxide and water) must be capable of representation by suitable modification of the above schemes. That the formation of the HO_2 complex does require a stabilising triple collision has been indicated by other workers (*e.g.*, Farkas and Sachsse, *ibid.*, 1934, *B*, **27**, 111).

Ritchie and Norrish (*Nature*, 1932, **129**, 243) reported that nitrogen had no appreciable effect on the quantum efficiency of hydrogen chloride formation in oxygen-rich mixtures. Their experiments were carried out with comparatively small pressures of nitrogen. The present paper constitutes an extension of these experiments, nitrogen, carbon dioxide, argon, neon, and helium being the gases investigated. The quantum efficiency of water formation may thus be expected to depend similarly on the addition of "inert" gas; measurements were therefore undertaken to determine the mechanism of hydrogen atom removal consistent with both hydrogen chloride and water formation.

Experimental.

(a) *Quantum Efficiency of Hydrogen Chloride Formation* (γ_{HCl}).—Use was made of the photometric method already described (Ritchie and Norrish, *Proc. Roy. Soc.*, 1933, *A*, **140**, 99), the "method of averaging" being adopted. Hydrogen and oxygen were obtained by electrolysis of potassium hydroxide solution, and cylinder chlorine was employed. Purification of these reactants and of the other gases was as already described (Ritchie and Norrish, *loc. cit.*; Ritchie, *ibid.*, 1934, *A*, **146**, 828). The soft-glass vessel, of approximately 35 c.c. volume, was spherical and attached to the Bourdon "sickle" gauge by a ground-glass joint lubricated by Apiezon grease L. Although the material of the reaction vessel may be of great importance in oxygen-free mixtures, where very high quantum efficiencies are to be expected (cf. Potts and Rollefson, *J. Amer. Chem. Soc.*, 1935, **57**, 1027), yet in oxygen-rich mixtures with quantum efficiencies of not more than 150, the effect of such factors appears to become inappreciable. The light source was an ordinary 500-watt lamp, run at 190 volts from 220-volt mains and controlled by a variable hand resistance. The white light from this lamp was employed in the actual photo-combination, and the chlorine concentration at the end of each period of illumination was determined by means of the light produced ($\gamma \doteqdot 3650$ A.) by inserting a plate of Chance's "ultraviolet" glass in the path of the light beam. Values of $\log I_0/I$, where I_0 is the transmitted intensity for zero chlorine pressure and I that for any other pressure, were then obtained by means of the photo-electric cell arrangement already described (Ritchie, *loc. cit.*), and compared with the values obtained by preliminary calibration for various chlorine pressures. The experimental system did not yield directly an exactly linear proportionality between $\log I_0/I$ and chlorine pressure in the range 0—100 mm., but the departure from linearity was small, and readings were sufficiently accurate for the purpose. The temperaure at which all experiments were carried out was 25°.

Results.—Quantum efficiencies $\gamma^{exp.}_{HCl}$ were calculated by the formula

$$\gamma^{exp.}_{HCl} = k \cdot 2\Delta\,[Cl_2]/t \cdot I_{abs.} \qquad (1)$$

where $\Delta[Cl_2]$ represents the decrease in chlorine pressure during the illumination by white light for t minutes, $I_{abs.}$ being the absorbed light expressed in galvanometer scale divisions, and calculated from the data of the chlorine concentration determination. Since the change in chlorine concentration involved was in general the same, and in other respects the light system was unaltered, relative quantum efficiencies are obtained by the above formula, although the actual illumination was carried out with white and not with "ultraviolet" light alone. Direct experiment showed that the addition of the various other gases did not appreciably alter the absorption of 3650 A. light; in view of the fact that the absorption coefficient of chlorine falls off rapidly as the wave-length increases, the use of white light for the actual illumination was not regarded as requiring in this connection any additional correction. In Table I are given details of a series of experiments on the variation of hydrogen pressure, the initial pressures of the other reactants being approximately the same in each experiment. In this and the following tables, $[Cl_2]$, [HCl], etc., represent the average concentration of reactants during the illumination; in all experiments where values of γ_{HCl} are recorded, no hydrogen chloride was present initially and $\Delta[Cl_2] = [HCl]$.

TABLE I.

γ_{HCl} : *Variation of* $[H_2]$.

$[Cl_2] \doteqdot 45$ mm., $[HCl] \doteqdot 10$ mm., $[O_2] \doteqdot 50$ mm.

$[H_2]$, mm.	$[Cl_2]$, mm.	$[O_2]$, mm.	t, mins.	[HCl], mm.	$I_{abs.}$, divs.	$\gamma^{exp.}_{HCl}$.	$\gamma^{calc.}_{HCl}$.	$\gamma^{exp.}_{HCl}/\gamma^{calc.}_{HCl}$.
453·9	45·5	51·3	25·25	8·4	15·1	53·3	53·2	1·00
398·3	45·7	50·7	25·0	8·6	14·2	58·6	59·2	0·99
338·3	45·4	51·1	25·0	10·5	14·9	68·3	64·0	1·06
333·1	46·8	50·4	17·0	7·8	15·6	71·3	69·2	1·03
222·8	45·7	50·7	19·0	9·6	14·8	82·6	84·3	0·98
56·8	45·4	51·0	13·5	10·9	15·0	130·2	134·0	0·97

Values of $\gamma^{exp.}_{HCl}$ were obtained by assigning the value $2{\cdot}43 \times 10^3$ to k in equation (1). $\gamma^{calc.}_{HCl}$ was obtained by means of the equation (Norrish and Ritchie, *loc. cit.*)

$$\gamma_{HCl} = \frac{3{\cdot}77 \times 10^4 \times [H_2] \times [Cl_2]}{[O_2]\{9{\cdot}25([Cl_2] + 1{\cdot}7[HCl]) + [H_2]([H_2] + 4[HCl] + 140)\}} \quad . \quad . \quad (2)$$

In effect, the absolute absorbed energy in these experiments was determined by comparison with the experiments of Norrish and Ritchie. Strictly, equation (2) refers to light of wave-length 3650 A.; this is not regarded as introducing any large error in the calculated "absolute" values for the wave-lengths effective under the above conditions of oxygen-rich mixtures (cf. Ritchie and Norrish, *Nature*, 1932, **129**, 243).

For the conditions in question, the first term of the denominator is small in comparison with the second; the probable error in the coefficient 1·7 (Potts and Rollefson, *loc. cit.*) does not here have appreciable significance. The ratios of the last column of the table confirm the use of equation (2) as an expression of the retarding effect of hydrogen.

Tables II and III give details of those experiments in which various gases were separately added. In all cases such addition resulted in a decreased quantum efficiency.

In the experiments of Table III, a tap was inserted between gauge and reaction vessel to prevent diffusion of chlorine from the non-illuminated gauge during the long time of illumination required for mixtures of high oxygen concentration. In control experiments for the conditions of Tables I and II, however, no difference in rate could be detected whether this tap was open or closed.

(b) *Quantum Efficiency of Water Formation* (γ_{H_2O}).—The method adopted was to introduce a small quantity of phosphoric oxide (B.D.H.) into the reaction vessel, the consequent decrease in pressure on illumination, due to formation and removal of water vapour, being recorded by means of the calibrated telescope-gauge-pointer system. One telescope scale division was equivalent to 0·0835 mm. at the pressures employed, readings being accurate to 0·1 division, *i.e.*, 0·0083 mm. The use of tap grease, and consequent absorption of chlorine and hydrogen chloride, necessitated a correction; this, however, was small in comparison with the total decrease (see Table IV) and was approximately the same both before and after the period of illumination. It was largely to minimise this correction that white light was employed, its use giving a relatively large decrease, due to formation of water, in a reasonable time of illumination. The normal "dark" decrease was not obtained immediately the light was cut off, several minutes being generally required for the complete removal of water vapour from the gas phase. A small graphical extrapolation was therefore used to determine the pressure at the actual end of the

TABLE II.

γ_{HCl} : *Variation of* $[N_2]$, $[CO_2]$, [A], [Ne], *and* [He].

$[[Cl_2] \doteqdot 45$ mm.; $[H_2] \doteqdot 55$ mm.; $[HCl] \doteqdot 10$ mm.; $[O_2] \doteqdot 50$ mm.

Added gas, mm.	$[H_2]$, mm.	$[Cl_2]$, mm.	$[O_2]$, mm.	t, mins.	[HCl], mm.	$I_{abs.}$, divs.	$\gamma^{exp.}_{HCl}$.	$\gamma^{calc.}_{HCl}$.	$\gamma^{exp.}_{HCl}/\gamma^{exp.}_{calc.}$.
				Addition of nitrogen.					
0·0	54·6	46·0	50·4	14·0	12·0	15·35	135·2	136·0	0·99
101·0	55·5	45·5	50·1	15·0	10·9	15·5	113·5	105·5	1·07
221·8	55·5	45·4	51·1	16·0	8·8	15·7	85·0	83·1	1·02
301·2	56·7	47·5	50·4	18·5	9·0	15·4	76·5	76·3	1·00
396·3	56·7	46·4	50·7	20·0	8·5	15·9	64·8	64·7	1·00
451·1	58·3	47·0	51·6	20·0	7·4	15·6	57·6	60·3	0·96
				Addition of carbon dioxide.					
121·0	55·0	45·6	51·0	22·0	9·9	13·6	80·3	75·7	1·06
178·0	54·0	45·2	50·8	28·0	10·5	13·75	66·1	62·0	1·06
230·1	55·9	45·6	50·5	30·0	9·2	14·0	53·1	54·7	0·97
305·3	56·4	46·4	50·9	30·0	8·2	14·3	46·5	46·3	1·00
				Addition of argon.					
101·0	55·3	45·8	50·0	15·0	10·4	14·8	113·6	115·2	0·99
201·0	56·3	45·5	51·2	16·0	9·4	14·65	97·2	101·3	0·96
301·3	54·3	45·3	50·6	19·0	10·6	14·5	93·5	89·7	1·04
399·0	55·9	45·7	50·6	19·0	9·3	14·45	82·3	82·0	1·00
449·6	57·0	46·1	50·5	18·0	8·9	15·2	79·1	79·3	1·00
				Addition of neon.					
0·0	55·1	45·4	49·2	12·0	10·9	15·8	139	139	1·00
181·7	55·2	45·5	50·3	14·5	10·5	14·4	122	118	1·00
263·8	55·3	44·2	51·4	15·0	10·5	15·9	107	106	1·01
302·5	56·7	45·0	50·9	14·0	10·0	16·5	105	106·5	0·99
0·0	55·4	44·4	50·0	13·0	11·0	15·6	131	134	0·98
387·5	57·8	45·5	51·1	16·0	9·7	14·9	98·6	101	0·98
449·9	54·8	45·4	50·3	16·0	10·4	15·85	99·5	98·4	1·01
				Addition of helium.					
0·0	56·0	45·6	50·1	12·0	10·3	15·6	133	139	0·96
247·4	54·7	45·1	51·0	13·0	9·7	15·9	114	115	0·99
321·1	55·2	45·2	50·1	13·0	9·5	15·8	112	113	0·99
395·1	55·0	45·8	50·3	13·0	9·3	15·7	111	109	1·02

illumination. On an average, five experiments were performed before the phosphoric oxide was replaced.

Details are given in Tables IV, V, and VI. In these experiments, the photo-electric cell

TABLE III.

γ_{HCl} : *Variation of* $[O_2]$.

$[Cl_2] \doteqdot 45$ mm.; $[H_2] \doteqdot 55$ mm.; $[HCl] \doteqdot 10$ mm.

$[H_2]$, mm.	$[Cl_2]$, mm.	$[O_2]$, mm.	t, mins.	[HCl], mm.	$I_{abs.}$, divs.	$\gamma^{exp.}_{HCl}$.	$\gamma^{calc.}_{HCl}$.	$\gamma^{exp.}_{HCl}/\gamma^{calc.}_{HCl}$.
55·2	45·6	49·8	15·0	10·3	12·25	136	139	0·98
54·8	45·3	150·5	40·0	10·0	15·2	39·9	39·4	1·01
52·1	44·1	97·2	45·0	13·4	12·2	59·1	61·7	0·96
54·8	45·7	249·6	80·0	9·8	14·8	20·0	20·9	0·96
55·2	44·8	50·9	20·0	11·3	10·5	130	132	0·99
55·2	45·0	201·3	90·0	10·7	10·6	27·2	26·9	1·01
54·7	45·7	252·1	90·0	9·6	12·4	20·8	20·8	1·00
55·8	46·8	298·0	90·0	8·1	12·6	17·3	17·3	1·00
55·7	45·6	50·8	15·0	10·2	12·25	135	137	0·99

arrangement was replaced by a Weston photronic cell and mirror galvanometer. The values of $\gamma^{exp.}_{HCl}$ and $\gamma^{exp.}_{H_2O}$ were obtained by the expressions (1) and

$$\gamma^{exp.}_{H_2O} = k \times \tfrac{2}{3} \times [A]/t \times I_{abs.} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

respectively, where $k = 295$, as obtained from the results of Table V, this value representing in effect the calibration of the light system on the basis of Norrish and Ritchie's equation (*loc. cit.*). [This value of k differs from that previously given (p. 859) because the intensity measurements were carried out by means of a photronic and not by a photo-electric cell.] Here $I_{abs.}$ is expressed

as on p. 859, and $\frac{2}{3}[\Delta]$ represents the pressure of water, in mm., produced by white light illumination over *t* minutes. $[\Delta] = 0{\cdot}0835\ (\Delta_1 - \Delta_2)$, where Δ_1 is the total and Δ_2 the "dark" decrease in pressure (both in telescope-scale divisions) over the time *t*.

The method of calculation must be modified for the experiments (*f*) and (*g*), where the actual light absorbed cannot be taken as proportional to that absorbed for 3650 A.; $I_{abs.}$ was here calculated from the simultaneously measured $d[HCl]/dt$ which is known to be directly proportional to it. γ_{HCl} was determined at the same time as γ_{H_2O} in the experiments denoted by corresponding numbers. That the presence of phosphoric oxide in the reaction vessel did not appreciably affect the results is evident from the figures of Table VI.

It will be observed that γ_{H_2O} increases rapidly with increasing $[H_2]$, and less rapidly with increasing [HCl], $[CO_2]$, $[N_2]$ and $[O_2]$, but is independent of $I_{abs.}$, and decreases with increasing $[Cl_2]$.

TABLE IV.

Expt.		$[Cl_2]$, mm.	$[H_2]$, mm.	$[O_2]$, mm.	[HCl], mm.	*t*, mins.	$I_{abs.}$, divs.	Δ_1.	Δ_2.	$\gamma^{exp.}_{H_2O}$.	$\gamma^{calc.}_{H_2O}$.	$\gamma^{calc.}_{H_2O} / \gamma^{exp.}_{H_2O}$.
					(*a*) *Variation of* $[H_2]$.							
1		42·8	41·2	40·5	14·3	6·00	8·50	2·30	0·36	0·63	0·65	1·03
2		41·6	53·5	40·0	15·1	6·50	8·10	2·70	0·25	0·76	0·78	1·02
3		42·0	150·0	40·3	14·6	8·00	8·30	5·15	0·16	1·23	1·23	1·00
4		41·7	305·5	40·6	15·0	12·0	8·32	8·90	0·24	1·43	1·51	1·06
5		42·1	510·2	41·0	13·8	14·0	8·05	11·05	0·28	1·57	1·66	1·06
					(*b*) *Variation of* $[O_2]$.							
6		42·5	42·9	46·4	14·0	6·00	8·73	2·13	0·12	0·63	0·67	1·07
7		42·9	43·2	49·5	15·5	6·00	12·2	3·00	0·21	0·62	0·68	1·08
8		43·0	43·2	126·8	14·5	15·00	12·2	8·33	0·45	0·71	0·70	0·99
9		44·5	43·8	231·8	13·6	7·00	12·6	4·20	0·28	0·73	0·72	0·99
10		43·5	43·9	304·1	14·0	8·00	12·2	4·95	0·24	0·79	0·75	0·95
11		42·7	43·3	402·2	14·8	9·00	12·4	5·63	0·27	0·79	0·82	1·04
					(*c*) *Variation of* [HCl].							
12		42·7	43·5	50·0	13·3	6·00	9·04	2·30	0·18	0·62	0·67	1·08
13		43·4	42·6	49·8	114·7	15·00	9·90	7·95	0·45	0·83	0·81	0·98
14		44·0	44·5	51·2	212·1	7·50	9·70	4·60	0·25	0·99	0·84	0·85
15		44·2	43·0	50·2	316·1	8·50	10·1	5·70	0·34	1·03	0·86	0·83
16		43·1	42·9	50·3	414·1	10·00	9·75	6·95	0·40	1·12	0·875	0·72
					(*d*) *Variation of* $[N_2]$.							
	$[N_2]$.											
17	0·0	43·5	43·0	50·6	13·0	5·75	9·40	2·30	0·13	0·66	0·66	1·00
18	202·0	43·2	44·2	50·2	12·7	9·50	9·30	4·35	0·20	0·77	0·77	1·00
19	304·1	44·0	44·4	51·0	12·0	11·0	9·50	5·05	0·11	0·78	0·79	1·01
20	437·0	43·9	42·5	39·1	15·4	13·0	8·80	6·00	0·42	0·80	0·79	0·99
					(*e*) *Variation of* $[CO_2]$.							
	$[CO_2]$.											
21	198·1	44·1	43·8	49·5	13·2	14·0	9·55	6·80	0·14	0·82	0·80	0·98
22	399·0	43·8	42·5	49·5	12·6	8·50	9·56	4·30	0·10	0·85	0·83	0·97
					(*f*) *Variation of* $I_{abs.}$.							
23		42·8	44·0	48·0	13·7	6·00	9·35	2·38	0·12	0·66	0·67	1·02
24		44·2	44·3	49·1	12·0	14·0	3·42	2·25	0·42	0·63	0·66	1·04
25		43·3	43·3	50·3	14·2	6·33	8·80	2·55	0·25	0·68	0·68	1·00
26		42·8	43·1	50·3	14·9	15·0	3·95	2·81	0·37	0·68	0·67	0·99
					(*g*) *Variation of* $[Cl_2]$.							
27		21·9	41·6	35·3	16·7	14·0	5·00	3·95	0·14	0·92	1·01	1·09
28		64·8	44·9	99·2	12·0	5·50	14·8	3·10	0·27	0·57	0·51	0·90
29		85·2	45·6	150·7	11·5	4·50	25·0	3·42	0·22	0·47	0·42	0·90
					(*h*) *Other experiments.*							
	$[N_2]$.											
30	0·0	45·5	300·2	301·8	12·5	9·00	9·40	7·65	0·27	1·44	1·54	1·07
31	289·0	43·4	300·6	50·9	14·0	8·00	9·00	5·90	0·20	1·30	1·57	1·21
32	152·1	43·8	300·0	52·3	11·4	14·0	9·00	10·85	0·10	1·40	1·54	1·10

TABLE V.

γ_{HCl} *in presence of* P_2O_5.

Expt.		$[Cl_2]$, mm.	$[H_2]$, mm.	$[O_2]$, mm.	[HCl], mm.	t, mins.	$I_{abs.}$, divs.	$\gamma_{HCl}^{exp.}$.	$\gamma_{HCl}^{calc.}$.	$\gamma_{HCl}^{calc.} / \gamma_{HCl}^{exp.}$.
6		42·5	42·9	46·4	14·0	6·00	8·73	158	149	0·94
7		42·9	43·2	49·5	15·5	6·00	12·2	125	137	1·09
8		43·0	43·2	126·8	14·5	15·00	12·2	46·7	47·6	1·02
17		43·5	43·0	50·6	13·0	5·75	9·40	142	140	0·99
12		42·7	43·5	50·0	13·4	6·00	9·04	146	139	0·95
13		43·4	42·6	49·8	114·7	15·0	9·90	53·3	51·5	0·97
	$[N_2]$, mm.									
18	202·0	43·2	44·2	50·2	12·7	9·50	9·30	84·5	85·5	1·01
19	304·1	44·0	44·4	51·0	12·0	11·00	9·50	67·7	69·8	1·03
20	437·0	43·9	42·5	39·1	15·4	13·00	8·80	71·4	75·5	1·06
32	152·1	43·8	300·0	52·3	11·4	14·00	9·00	53·3	53·0	0·99
	$[CO_2]$, mm.									
21	198·1	44·1	43·8	49·5	13·2	14·00	9·55	58·2	60·0	1·03

TABLE VI.

γ_{HCl} *in absence of* P_2O_5.

43·4	45·6	42·0	14·9	6·16	8·60	161	164	1·02
43·3	45·5	92·2	12·8	12·1	8·50	73·6	71·0	0·97

DISCUSSION.

The decrease in pressure on illumination in the presence of phosphoric oxide has been attributed to the formation and removal of water vapour alone, no account being taken of the possible formation of other compounds. Illuminated mixtures of chlorine and oxygen showed no appreciable decrease in pressure which could be of importance in this connection. In hydrogen–chlorine–oxygen mixtures the formation of ClO would not involve in itself a decrease in pressure, although this is to be expected for ClO_2; since, however, these substances do not accumulate, they are presumably at once decomposed by illuminated chlorine. Hydrogen peroxide can be isolated under special conditions (Norrish, *Trans. Faraday Soc.*, **1931**, **27**, **461**), although again the amount in ordinary circumstances is very small; moreover, this, too, is decomposed by illuminated chlorine (Bodenstein and Schenk, *loc. cit.*). Consequently, it has been assumed that practically all the hydrogen peroxide formed is converted at once into water. The agreement between values of γ_{HCl} in the presence and in the absence of phosphoric oxide (Tables V and VI) seems to show that the use of the oxide is otherwise free from objection, except possibly with high pressures of hydrogen chloride, where a small absorption by " moist " oxide is not unexpected. This would partly be included in the " dark " correction: actually, comparison of calculated and experimental results (Table IV, *c*) shows a tendency which may be ascribed to this absorption. The experimental values of γ_{H_2O} are in this case maximum values, but the divergence does not sensibly affect the following arguments.

The mechanism adopted to represent the formation of hydrogen chloride and water in such oxygen-rich mixtures is as follows:

$$Cl_2 + h\nu = Cl + Cl \quad \dots \quad k_1$$
$$Cl + H_2 = HCl + H \quad \dots \quad k_2$$
$$H + Cl_2 = HCl + Cl \quad \dots \quad k_3$$
$$H + O_2 + H_2 = H_2O + OH \quad \dots \quad k_4$$
$$H + O_2 + Cl_2 = HCl + ClO_2 \quad \dots \quad k_5$$
$$H + O_2 + HCl = HO_2 + HCl \quad \dots \quad k_6$$
$$H + O_2 + M = HO_2 + M \quad \dots \quad k_M$$
$$HO_2 + H_2 = H_2O + OH \quad \dots \quad k_7$$
$$HO_2 + Cl_2 = HCl + ClO_2 \quad \dots \quad k_8$$

M may be oxygen or any of the indifferent gases mentioned in Table II. Application of the usual methods gives

$$\gamma_{HCl} = k_1 + \frac{2k_1k_3[Cl_2]}{k_4[O_2]\left[[H_2] + \frac{k_5}{k_4}[Cl_2] + \frac{k_6}{k_4}[HCl] + \frac{k_M}{k_4}[M]\right]} \quad . \quad . \quad . \quad (4)$$

$$\gamma_{H_2O} = \frac{k_1\left[[H_2] + \frac{\left(\frac{k_6}{k_4}[HCl] + \frac{k_M}{k_4}[M]\right)}{\left(1 + \frac{k_8}{k_7}\frac{[Cl_2]}{[H_2]}\right)}\right]}{\left[[H_2] + \frac{k_5}{k_4}[Cl_2] + \frac{k_6}{k_4}[HCl] + \frac{k_M}{k_7}[M]\right]} \quad . \quad . \quad . \quad . \quad . \quad . \quad (5)$$

As Norrish and Ritchie have shown (*loc. cit.*), expression (4) is not quite correct when the pressure of hydrogen is low, in that the denominator must be increased by a term involving $[Cl_2]/[H_2]$. Similar remarks apply therefore to expression (5); for simplicity, however, this correction, amounting to a maximum of about 5% in the final calculated efficiency, has here been omitted.

The efficiencies given in the tables have been calculated by making use of the following values : $k_1 = 2{\cdot}0$, $2k_1k_3/k_4 = 3{\cdot}77 \times 10^4$, $k_6/k_4 = 4{\cdot}00$ (Norrish and Ritchie), $k_{O_2}/k_4 = 0{\cdot}43$, $k_{Cl_2}/k_4 = 2{\cdot}64$, $k_{CO_2}/k_4 = 1{\cdot}65$, $k_{N_2}/k_4 = 0{\cdot}74$, $k_A/k_4 = 0{\cdot}43$, $k_{Ne}/k_4 = 0{\cdot}22$, $k_{He}/k_4 = 0{\cdot}18$, $k_8/k_7 = 1{\cdot}20$.

The last column of each table shows that experimental results for both γ_{HCl} and γ_{H_2O} are reasonably represented by the above scheme. Expression (4), when applied to the original results of Norrish and Ritchie, gives an agreement between experimental and calculated values which is as good as that shown by their earlier formula. There thus seems little doubt that the action of indifferent gases is directly connected with the stabilisation of the HO_2 complex, and that this does not appreciably react further, under the above conditions, in the propagation of the reaction chains. The fact that oxygen can act as an energy acceptor in this connection means that the rate of hydrogen chloride formation is inversely proportional to the concentration of oxygen in an intermediate region which passes, on the one side, at low oxygen concentrations into the " transition " region, and on the other, to a region where the rate is less than would be expected on the basis of such inverse proportionality.

Table VII shows also relative values of coefficients already determined for other triple collisions, the nitrogen coefficient being taken as unity. These refer to concentrations in mm.

TABLE VII.

Relative Triple Collision Coefficients.

Reaction.	HCl.	Cl_2.	CO_2.	O_2.	N_2.	A.	Ne.	He.	H_2.
1. Br + Br			2·16	1·28	1·00	0·52		0·30	0·85
2. Br + Br			1·38	1·38	1·00	0·64		0·41	0·51
3. I + I			2·72	1·59	1·00	0·58		0·27	0·61
4. Cl + NCl_3		2·24	2·24	1·47	1·00	0·94		0·55	0·55
5. H + O_2	5·4	3·57	2·23	0·58	1·00	0·60	0·30	0·24	1·35
6. O + O_2				0·44	1·00	0·63			
7. O + O_2			2·0	2·0	1·00	0·2		0·4	
8. H + H						0·60	0·22	0·06	0·06

1. Rabinowitch and Wood, *Trans. Faraday Soc.*, 1936, **32**, 907.
2. Ritchie, *Proc. Roy. Soc.*, 1934, *A*, **146**, 828.
3. Rabinowitch and Wood, *J. Chem. Physics*, 1936, **4**, 497.
4. Griffiths and Norrish, *Trans. Faraday Soc.*, 1931, **27**, 451; *Proc. Roy. Soc.*, 1934, *A*, **147**, 143.
5. Present results
6. Ritchie, *Proc. Roy. Soc.*, 1934, *A*, **146**, 848.
7. Schumacher and Beretta, *Z. physikal. Chem.*, 1932, *B*, **17**, 417.
8. Senftleben and Hein, *Ann. Physik*, 1935, **22**, 1. No value for nitrogen was determined: the argon coefficient has here been put equal to 0·60 and the other values calculated accordingly.

In the reactions in which only a simple stabilising collision seems possible, efficiencies fall into a well-defined series $CO_2 > N_2 > A > Ne > He$. On this basis the relatively high

efficiency of hydrogen for the HO_2 reaction is then due to the fact that the triple collision *between H, O_2, and H_2 does not involve stabilisation of the HO_2 complex.* It should be pointed out that the same formula for γ_{HCl} and γ_{H_2O} may be obtained if

$$H + O_2 + H_2 = H_2O + OH \quad (4)$$

and

$$HO_2 + H_2 = H_2O + OH \quad (7)$$

are replaced by, respectively,

$$H + O_2 + H_2 = H_2O_2 + H \quad (4')$$

and

$$HO_2 + H_2 = H_2O_2 + H \quad (7')$$

where the subsequent reaction $H_2O_2 + Cl = ClO + H_2O$ must be taken to represent the chain-ending process which undoubtedly occurs in the presence of hydrogen and nitrogen. That hydrogen peroxide is rapidly removed by illuminated chlorine has been already proved (see p. 862). Present results therefore do not distinguish between reactions (4) and (4′). No values of γ_{H_2O} greater than 2 have here been recorded, even with high concentrations of hydrogen, where mutual recombination of OH radicals might occur with subsequent formation of water. The results of Bodenstein and Schenk confirm this, with one exception which is perhaps due to experimental error, since other experiments with similar concentrations give values less than 2. The results of Krauskopf and Rollefson (*loc cit.*) on the ratio of hydrogen used up in water formation to total hydrogen disappearing on illumination are in agreement with this conception that, if the hydroxyl radical is formed, it does not eventually give water under these conditions. Similarly, Chapman and Watkins (J., 1933, 744) conclude that the quantum efficiency of water formation may rise as high as 2. If reaction (4) be the true one, the hydroxyl radicals must be effectively removed before a process eventually involving the formation of water can take place. Possibilities are

$$OH + Cl_2 = HCl + ClO - 9{\cdot}5 \text{ kg.-cals.} \quad (a)$$

and

$$OH + Cl = HCl + O - 2{\cdot}5 \text{ kg.-cals.} \quad (b)$$

Although reaction (*a*) is more strongly endothermic, reaction (*b*) is probably of less importance here, since its rate depends on the product of two very small concentrations and would involve an $(I_{abs.})^{\frac{1}{2}}$ term in the expression for γ_{HCl}, contrary to experiment.

The triple collision between H, O_2, and HCl appears to be a simple stabilising one, contrary to previous supposition; since $k_{HCl}/k_4 = 4{\cdot}00$, γ_{H_2O} would increase very rapidly with increasing pressures of hydrogen chloride if this triple collision yielded water and ClO. Calculated values of γ_{H_2O} in this series are very sensitive to the value of k_8/k_7, representing the rates of reaction of HO_2 with chlorine and hydrogen: it is to be noted that it differs considerably from the ratio k_5/k_4, although there is no immediate reason why these ratios should be identical. The ratio k_5/k_4 is perhaps liable to greater experimental error than usual in that the experimental arrangements did not permit of its more accurate determination with higher pressures of chlorine. The experimental values of γ_{H_2O} at high chlorine pressures are greater than calculated values; this may be partly due to the formation of ClO_2, for which no allowance has been made.

The thermal data of these reactions have already been discussed by Bodenstein and Schenk (*loc. cit.*, p. 435), who show that reactions (7) and (8) are exothermic if the $H + O_2$ reaction produces not more than 44 kg.-cals. Table VIII shows the data of the first ten

TABLE VIII.

No.	$[Cl_2]$, mm.	$[H_2]$, mm.	$[O_2]$, mm.	[HCl], mm.	$\gamma^{exp.}_{H_2O}$	$\gamma^{calc.}_{H_2O}$	$\gamma^{calc.}_{H_2O}/\gamma^{exp.}_{H_2O}$
1	103·5	372	202	70·4	0·49	1·28	2·62
2	86·5	332	201	151	1·00	1·37	1·37
3	61·4	285	193	221	1·65	1·53	0·93
4	32·0	256	187	256	1·71	1·69	0·99
5	59·4	432	228	44·4	1·23	1·55	1·26
6	59·7	392	218	90·0	1·23	1·55	1·26
7	41·8	381	220	116	1·99	1·67	0·84
8	28·4	378	218	120	2·58	1·76	0·68
9	26·2	365	212	130	1·68	1·77	1·05
10	29·9	394	223	112	1·27	1·75	1·38

of the 22 experiments carried out by those authors (*loc. cit.*, p. 427) at 60° by a flow method involving no phosphoric oxide in the illuminated vessel. The concentrations have been converted from millimoles/l. to mm.; in the penultimate column are given values calculated by the present formula (5) for γ_{H_2O}.

In view of the experimental error apparently involved, there is a reasonable agreement between $\gamma^{calc.}_{H_2O}$ and $\gamma^{exp.}_{H_2O}$, as shown by the ratios in the last column, which average 1·08 if experiment 1 is ignored. In general, the results of Bodenstein and Schenk are lower than those calculated by the present formula (5), more especially when the $[Cl_2]/[H_2]$ ratio is relatively large; the discrepancy is then due probably to the neglect of the term involving $[Cl_2]/[H_2]$ in the denominator (see p. 863), corresponding to the breaking of the reaction chains by removal of chlorine atoms as well as by removal of hydrogen atoms.

SUMMARY.

Measurements have been made of the relative quantum efficiencies of hydrogen chloride and water formation in certain hydrogen–chlorine–oxygen mixtures. The quantum efficiency of hydrogen chloride formation is reduced by the addition of carbon dioxide, nitrogen, argon, neon, and helium; that of water formation increases with increasing pressure of hydrogen, less rapidly with increasing pressures of hydrogen chloride, oxygen, carbon dioxide, and nitrogen, but is independent of the light energy absorbed and decreases with increasing pressure of chlorine. A mechanism is discussed which is consistent for both hydrogen chloride and water formation, where the actions of hydrogen chloride, oxygen, carbon dioxide, nitrogen, argon, neon, and helium are related to the stabilisation of the HO_2 complex in a triple collision.

UNIVERSITY OF SHEFFIELD. [*Received, December 1st, 1936.*]

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179. *A New Calcium Silicophosphate.*

By GUNTER NAGELSCHMIDT.

IN the course of a mineralogical investigation of a typical series of modern basic slags which had been tested as phosphatic fertilisers in field and pot culture experiments (Crowther, *J. Roy. Agric. Soc.*, 1934, **95**, 1), a new material was found as a major constituent of some open-hearth slags with citric acid solubilities between 40 and 80%. Although at least 80% of the material in commercially ground basic slags is guaranteed to pass through the British Standard Test Sieve, mesh number 100, a few individual particles may be as large as 0·5 mm. in diameter and a small fraction is below the range of microscopic visibility. Most of the grains are heterogeneous; they contain inclusions, different materials are intergrown, and it is therefore very difficult to isolate the pure components, although these can often be recognised and identified by microscopical and microchemical methods. In the present work it was possible to isolate the new compound in three stages.

(1) A suitable grain size group of about 0·2—0·02 mm. diameter was separated by sieving and sedimentation in water saturated with calcium carbonate. (2) A magnetic separation was carried out by using Hallimond's separator (*Min. Mag.*, 1930, **22**, 377),* a non-magnetic fraction being obtained in which all the grains were more or less free from dark inclusions. (3) A gravity separation was effected by repeated centrifuging with methylene iodide–benzene mixtures. The new compound was found to have $d^{20°}$ 3·035 ± 0·005.

Optical Properties.—The material is colourless, and biaxial positive. The angle of the optical axes is very small. The largest and the smallest refractive indices observed with sodium light are n_γ 1·661 and n_α 1·652 ± 0·002. The grains frequently have two opposite parallel edges with straight extinction along these edges. No other crystallographic boundaries occur, and the crystal symmetry is unknown, but cannot be higher than orthorhombic.

Chemical Composition.—From 25 g. of slag the above method of separation afforded a 0·5 g. fraction which seemed to be sufficiently pure for chemical analysis, although it still contained a small percentage of foreign materials. Analyses made on 127 and 234 mg. gave the results shown

* The author is indebted to Prof. P. G. H. Boswell for permitting him to use this apparatus at the School of Mines of the Imperial College of Science and Technology.

in Table I, (i) and (ii) respectively, which give $CaO : P_2O_5 : SiO_2$ = approx. 7 : 1 : 2. If a recalculation is made on this basis it appears that the analysed material contained 92% of this compound, contaminated with tricalcium silicate and some spinelloid material. In view of this contamination and the fact that the analyses account only for 97% of the material, the formula of the new compound cannot be established with certainty, but $7CaO,P_2O_5,2SiO_2$ seems the most probable.

Körber and Trömel (*Arch. Eisenhüttenw.*, **1933**, **7**, 7), investigating the ternary system CaO–P_2O_5–SiO_2, found two ternary compounds. The first had the composition $5CaO,SiO_2,P_2O_5$ and was identical with silicocarnotite, which has long been known as the main constituent of basic Bessemer slags. To the second compound they ascribed the composition $9CaO,P_2O_5,3SiO_2$, but later (Trömel, private communication), $8CaO,P_2O_5,2{\cdot}5SiO_2$ was found to agree better with the data. It is not yet known, however, how far this second compound is able to form mixed crystals with the other components of the ternary system, and further synthetic work will be needed to elucidate this point. Both ternary compounds had citric acid solubilities above 95%.

The author is much indebted to Dr. Trömel for supplying him with a sample of his second ternary compound, which proved to have very similar optical properties to those described for the material $7CaO,P_2O_5,2SiO_2$ isolated as detailed above. *X*-Ray powder diagrams * of the two materials proved to be identical, both in the position and in the intensities of the lines. The data are in Table II, together with comparable data for silicocarnotite, which gave a different pattern. This proves that the new compound is not a mixed crystal of silicocarnotite and dicalcium silicate. In view of the low crystal symmetry, the complex chemical composition, and the absence of suitably formed single crystals, no attempt was made to determine the crystal structure of the new material from the *X*-ray data.

TABLE I.

Chemical analysis of new compound.

	(i).	(ii).	Calc. for $7CaO,2SiO_2,P_2O_5$.
CaO, %	58·3	58·4	60·0
P_2O_5, %	19·9	20·0	21·6
SiO_2, %	17·9	17·7	18·4
$Fe_2O_3 + Al_2O_3$, %	—	0·4	—
MgO, %	—	0·6	—
Total, %	96·1	97·1	100·0

TABLE II.

Powder diagrams of silicocarnotite (I), the new compound (II), and Trömel's synthetic material (III), taken with copper *K*-α radiation; interplanar spacings (*d*) and intensities (*I*) are recorded.

	(I).		(II).		(III).	
No.	*d.*	*I.*	*d.*	*I.*	*d.*	*I.*
1	4·58	w.	3·93	w.	3·93	w.
2	3·96	m.	3·51	w.	3·52	w.
3	3·60	v.w.	2·85	s.	2·86	s.
4	3·33	m.	2·70	s.	2·70	s.
5	2·99	m.	2·33	v.w.	2·33	v.w.
6	2·83	v.s.	2·22	v.w.	2·24	v.w.
7	2·61	v.s.	1·960	s.	1·961	s.
8	2·29	m.	1·862	v.w.	1·862	w.
9	2·18	m.	1·761	m.	1·761	m.
10	2·03	w.	1·668	w.	1·666	w.
11	1·958	w.	1·591	w.	1·590	w.
12	1·880	s.	1·562	w.	1·562	w.
13	1·812	w.	1·485	m.	1·487	m.
14	1·750	m.	1·346	m.	1·347	m.
15	1·691	m.	1·260	v.w.	1·262	v.w.
16	1·644	v.w.	1·220	v.w.	1·219	v.w.
17	1·538	w.	1·185	v.w.	1·185	v.w.
18	1·510	w.				
19	1·241	w.				
20	1·159	w.				
21	1·136	w.				
22	1·046	v.w.				
23	1·030	v.w.				

v.s. = very strong, s. = strong, m. = medium, w. = weak, v.w. = very weak.

* The author's thanks are due to Sir William Bragg and the Managers of the Royal Institution for facilities of the Davy Faraday Research Laboratory.

SUMMARY.

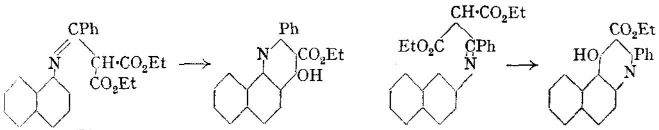
A new compound has been isolated from certain medium-soluble open-hearth basic slags, with a chemical composition approximating to $7CaO,P_2O_5,2SiO_2$. It has $d^{20°}$ 3·035, n_γ 1·661, n_α 1·652 for sodium light, and is colourless and biaxial positive with a very small axial angle. *X*-Ray powder data are given. This material is almost identical with a synthetic calcium silicophosphate of approximate composition $8CaO,P_2O_5,2·5SiO_2$ prepared by Trömel.

ROTHAMSTED EXPERIMENTAL STATION, HARPENDEN. [*Received, January 12th*, 1937.]

180. *Imidochlorides. Part V. Synthesis of Hydroxycarbethoxyphenyl-α- and -β-naphthaquinolines.*

By V. R. HEERAMANECK and R. C. SHAH.

ETHYL α- and β-naphthyliminobenzylmalonate (I and II respectively), prepared by the authors' modification (J., 1936, 428) of Just's method (*Ber.*, 1886, **19**, 984, 987), have been cyclised by the action of heat to *ethyl 4-hydroxy-2-phenyl-α-naphthaquinoline-3-carboxylate* (III) and *ethyl 1-hydroxy-3-phenyl-β-naphthaquinoline-2-carboxylate* (IV) respectively.



(I.) (III.) (II.) (IV.)

As β-naphthylamine usually undergoes ring closure in the α-position (Lellmann and Schmidt, *Ber.*, 1887, **20**, 3154; von Braun and Gruber, *Ber.*, 1922, **55**, 1710), the β-naphthaquinoline derivative has been assigned the structure (IV).

A mixture of benz-α-naphthalide imidochloride [from benz-α-naphthalide (30 g.; 1 mol.) and phosphorus pentachloride (30·5 g.; 1·2 mols.)], ethyl malonate (23 g.; 2 mols.), and sodium (1·5 g.; 1 atom) was refluxed in anhydrous toluene at 120—130° for 2 hours and treated with water; the product extracted by ether was heated at 120—125°/30—40 mm. to remove toluene and the excess of malonic ester; the residual ethyl α-naphthyliminobenzylmalonate, after solidifying, crystallised from alcohol in needles, m. p. 146—148° (Just, *loc. cit.*, gives m. p. 144°). Yield, 8 g. (17·5%).

This ester (1·5 g.) was heated at 185—195° until the evolution of bubbles of ethyl alcohol could be noticed. The resulting *ethyl 4-hydroxy-2-phenyl-α-naphthaquinoline-3-carboxylate* (III) crystallised from ethyl acetate in needles, m. p. 228—230° (Found: N, 4·3. $C_{22}H_{17}O_3N$ requires N, 4·0%), difficultly soluble in hot methyl and ethyl alcohols and chloroform, and insoluble in benzene, toluene, and light petroleum.

Ethyl β-naphthyliminobenzylmalonate, prepared from benz-β-naphthalide imidochloride (19 g.; 1 mol.), ethyl malonate (23 g.; 2 mols.), and sodium (1·5 g.; 1 atom), crystallised from alcohol in needles, m. p. 141—142° (Just, *loc. cit.*, gives m. p. 140°). Yield, 8 g. (29·6%).

This ester (4 g.), heated at 185—195°, gave *ethyl 1-hydroxy-3-phenyl-β-naphthaquinoline-2-carboxylate* (IV), which crystallised from alcohol in needles (3 g.), m. p. 280—282° (Found: N, 4·3%), and resembled the α-naphthaquinoline derivative in solubility. It gave, on hydrolysis with aqueous alcoholic caustic soda, the *acid*, which crystallised from alcohol in needles, m. p. 248—250° (Found: N, 4·4. $C_{20}H_{13}O_3N$ requires N, 4·5%), and, when refluxed with alcoholic picric acid for 3 hours, formed a *picrate*, which separated in orange needles, m. p. 179—181°, on cooling (Found: N, 10·1. $C_{22}H_{17}O_3N,C_6H_3O_7N_3$ requires N, 9·8%).

ROYAL INSTITUTE OF SCIENCE, BOMBAY. [*Received, April 12th*, 1937.]

181. *The Formation of Organo-metalloidal and Similar Compounds by Micro-organisms. Part V. Methylated Alkyl Sulphides. The Fission of the Disulphide Link.*

By FREDERICK CHALLENGER and ALAN A. RAWLINGS.

EARLIER communications have established the methylating action of *Penicillium brevicaule* (*Scopulariopsis brevicaulis*) *Saccardo* on inorganic and organic compounds of arsenic (J., 1933, 95; 1935, 396; 1936, 264; *Biochem. J.*, 1935, **29**, 1757) and on inorganic compounds of selenium (J., 1934, 68). In the memoir last cited, it was mentioned that no methylation could be observed with sulphur or with several of its common inorganic and organic compounds, including thiourea.

This was somewhat surprising in view of the experiments of Pohl (*Arch. exp. Path. Pharm.*, 1904, **51**, 341), who noticed a leek-like odour in the expired air of animals receiving subcutaneous or intravenous injections of thiourea. The odorous product was non-reactive to sodium hydroxide or mercuric cyanide, and was therefore not a mercaptan. It was, however, absorbed by sulphuric acid and gave a precipitate with mercuric chloride which, on oxidation, yielded a sulphate. Pohl therefore concluded that the product was an alkyl sulphide. Hofmeister (*ibid.*, 1894, **33**, 198) observed the formation of an odorous tellurium compound, assumed to be dimethyl telluride, in the breath of dogs after injections of potassium tellurite. This work and the similar animal experiments of Maassen with selenites (*Arb. Kaiserl. Ges. Amt.*, 1902, **18**, 475) have been critically discussed by one of us (*Chem. and Ind.*, 1935, **54**, 657). Hofmeister was, however, unable to detect any odour in the expired air of dogs and rabbits fed with powdered sulphur or injected with sodium sulphide or thiosulphate.

Neuberg and Grosser (*Centr. Bl. Physiol.*, 1905-6, **19**, 316) stated that the precursor of the diethyl sulphide which was shown by Abel (*Z. physiol. Chem.*, 1894, **20**, 253) to be evolved on warming the urine of dogs with alkali is methyldiethylsulphonium hydroxide. They also state that administration of diethyl sulphide to dogs gives rise to this compound, but experimental details have not been published.

Particular interest attaches to the observation of Haas (*Biochem. J.*, 1935, **29**, 1298) that the seaweeds *Polysiphonia fastigiata* and *P. nigrescens* evolve dimethyl sulphide shortly after being gathered. The occurrence in nature of methylated compounds of sulphur such as cheirolin, $CH_3{\cdot}SO_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}NCS$, erysolin, $CH_3{\cdot}SO_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}NCS$ (see Armstrong and Armstrong, "The Glycosides," 1931, p. 66, for references), and particularly methionine, $CH_3{\cdot}S{\cdot}CH_2{\cdot}CH_2{\cdot}CH(NH_2){\cdot}CO_2H$, demonstrates the possibility of a biological methylation of sulphur. The relation of methionine to cysteine and to cystine suggested that compounds containing the –SH or –S–S– links might be more amenable to the methylating action of the mould.

Neuberg and Schwenk (*Biochem. Z.*, 1915, **71**, 118) showed that, on addition to a solution of sugar undergoing fermentation by bottom yeast, diethyl disulphide is reduced to ethyl mercaptan.

Dr. H. E. North (unpublished observation) found that on addition of diethyl disulphide to bread cultures of *P. brevicaule*, ethyl mercaptan was evolved; it was identified as the mercaptide, $Hg(SEt)_2$, by absorption in mercuric cyanide. The gases issuing therefrom reacted with mercuric chloride, giving a precipitate which was clearly a mixture. Diethyl disulphide, b. p. 153°, is volatile in a stream of air and, as it is inert to mercuric cyanide, any which escaped reaction in the culture flasks would reach the mercuric chloride.

Morin (*Pogg. Annalen*, 1839, **48**, 483) and Otto (*Ber.*, 1882, **15**, 125) mention the formation of a heavy white crystalline precipitate from diethyl disulphide and alcoholic mercuric chloride, but give no further details.

The behaviour of aliphatic disulphides R·S·S·R (R = Et or *n*-Pr) with excess of saturated aqueous mercuric chloride was therefore examined. In each case a white insoluble precipitate of the composition $R{\cdot}S{\cdot}HgCl,HgCl_2$ was formed. Its weight accounted for only about 70% of the disulphide, the remainder having formed soluble products (see p. 869). The insoluble compounds were shown by analysis, m. p. and mixed m. p. to be identical with

those obtained from the corresponding mercaptans and excess of aqueous mercuric chloride. The information obtainable from the literature regarding the last reaction is incomplete. Bertram (*Ber.*, 1892, **25**, 64) obtained CH_3·S·HgCl from methyl mercaptan. The product formed from ethyl mercaptan in alcoholic solution is stated by Debus (*Annalen*, 1849, **72**, 18) to be Et·S·HgCl, but no mention of a double compound with mercuric chloride is made. Sachs (*Ber.*, 1921, **54**, 1849), who obtained Et·S·HgCl from ethyl thioacetate, CH_3·CO·SEt, mercuric acetate, and sodium chloride, states that with mercuric chloride in ether it is converted into Et·S·HgCl,$HgCl_2$. We have observed that the same addition takes place slowly in aqueous solution.

We find that when ethyl or *n*-propyl mercaptan reacts with suitable quantities of aqueous mercuric chloride, any one of the three compounds $(RS)_2Hg$, R·S·HgCl, and R·S·HgCl,$HgCl_2$ may be isolated at will. The formation of the mercaptides $(RS)_2Hg$ under these conditions does not appear to have been described, these compounds being usually obtained from mercuric oxide or cyanide.

The soluble products from the interaction of diethyl disulphide and mercuric chloride, which will be described in a later communication, presumably arise from the decomposition of the sulphenic acid, Et·S·OH, produced thus:

$$\text{(I)}\quad 2Et{\cdot}S{\cdot}SEt + 4HgCl_2 = 2Et{\cdot}S{\cdot}HgCl,HgCl_2 + 2Et{\cdot}SCl$$
$$\text{(II)}\quad 2Et{\cdot}SCl + 2HOH = 2Et{\cdot}S{\cdot}OH + 2HCl$$

The weights of chloromercury ethylthiol mercurichloride obtained in this reaction and the general properties of the aromatic chlorothiols R·SCl (Zincke and Farr, *Annalen*, 1912, **391**, 57; the corresponding aliphatic compounds have not been isolated) are in agreement with the following scheme for the further reaction:

$$\text{(III)}\quad 2Et{\cdot}S{\cdot}OH = Et{\cdot}SH + Et{\cdot}SO_2H\text{ ; (IV)}\quad Et{\cdot}SH + 2HgCl_2 = Et{\cdot}S{\cdot}HgCl,HgCl_2 + HCl$$

$$\text{Summarised: }\quad 2Et{\cdot}S{\cdot}SEt + 6HgCl_2 + 2H_2O = 3Et{\cdot}S{\cdot}HgCl,HgCl_2 + Et{\cdot}SO_2H + 3HCl$$

The sulphenic and the sulphinic acid may react, giving diethyl disulphoxide thus:

$$Et{\cdot}S{\cdot}OH + Et{\cdot}SO_2H = H_2O + Et{\cdot}SO_2{\cdot}SEt$$

and the sulphinic acid may give disulphoxide and sulphonic acid (Otto and Rössing, *Ber.*, 1886, **19**, 1235; von Braun and Weissbach, *Ber.*, 1930, **63**, 2836).

Since the double compounds R·S·HgCl,$HgCl_2$ would clearly be formed in the mercuric chloride absorption bottles during experiments with the mould and R·S·SR, their properties were studied.

On boiling with water a molecule of mercuric chloride is removed, and an insoluble solid R·S·HgCl (in the case of the ethyl derivative, unmelted at 250°) obtained. This is almost unaffected by cold sodium hydroxide, but on warming, mercuric oxide and sodium alkyl mercaptide are produced. Hydrochloric acid gives the mercaptan at once, as also with R·S·HgCl,$HgCl_2$. Neither R·S·HgCl,$HgCl_2$ nor R·S·HgCl liberates any mercaptan when warmed with sodium hydroxide in an air stream, aspiration through mercuric cyanide giving no precipitate.

The fission of the disulphides under the influence of mercuric chloride is in accord with many other of their reactions. For instance, alkyl iodides give trialkylsulphonium iodides and tri-iodides (Davies, *Ber.*, 1891, **24**, 3548; Hilditch and Smiles, J., 1907, **91**, 1397; Steinkopf and Müller, *Ber.*, 1923, **56**, 1926); ethylmagnesium bromide with diethyl disulphide gives ethyl sulphide and ethyl mercaptan (Baroni, *Atti R. Accad. Lincei*, 1930, **11**, 905); nitrated aryl disulphides and chlorine yield the corresponding chlorothiols R·SCl (Zincke *et al.*, *Annalen*, 1913, **400**, 6, 11; 1918, **416**, 95). The fission of alkyl and aryl disulphides by chloramine-T (Alexander and McCombie, J., 1932, 2087) should also be mentioned.

The work of Schönberg (*Ber.*, 1935, **68**, 163 and earlier references) shows that the aromatic disulphides must be regarded as undergoing dissociation to the free radical RS.

The behaviour of disulphides to mercuric chloride having been established, diethyl and di-*n*-propyl disulphides were added in dilute aqueous suspension to the bread cultures.

In each case the products issuing from the culture flasks consisted of the mercaptan

R·SH, the unchanged disulphide R·S·SR, and the methyl alkyl sulphide, R·S·CH_3. In the case of the relatively non-volatile di-*n*-propyl disulphide very little of this came over. The precipitates in the mercuric chloride flasks consisted of mixtures of the mercuric chloride addition product of the methyl alkyl sulphide with various amounts of R·S·HgCl,$HgCl_2$. On treatment of these mixtures with sodium hydroxide in a slow stream of air pure methyl alkyl sulphide was evolved and converted into the mercurichloride. No mercaptan volatilised in these circumstances (see p. 869). The methyl alkyl sulphides were also characterised as the benzylmethylalkylsulphonium picrates, and (in the case of methyl ethyl sulphide) as the double compound with platinous chloride.

All these derivatives were compared with authentic specimens. The compounds not previously described were: *chloromercury* n-*propylthiol mercurichloride*, Pr^{a}·S·HgCl,$HgCl_2$; *methyl ethyl sulphide dimercurichloride*, Me·SEt,$2HgCl_2$; *benzylmethylethylsulphonium picrate* and *benzylmethyl*-n-*propylsulphonium picrate*.

In view of the reducing properties of cultures of *P. brevicaule* (*Biochem. J.*, 1935, **29**, **1763**; J., 1935, 396) the formation of mercaptans from the disulphides was not surprising. Addition of ethyl and *n*-propyl mercaptans to bread cultures of the mould under the same conditions as obtained for the disulphides gave very similar results, methylation being observed in each case.

As regards the mechanism of the methylation and reduction of the disulphides, it appeared possible that some such reaction as R·S·SR + $2CH_2O$ = R·S·CH_3 + R·SH + CO_2 might occur. If so, the ratio of methyl alkyl sulphide to mercaptan should be at least 1 : 1; allowing for some possible methylation of the mercaptan, an even higher ratio might be expected. This, however, is not the case. By weighing the alkyl mercaptides $Hg(SR)_2$ and the methyl alkyl sulphide mercurichlorides it was shown in preliminary experiments that the mercaptan is produced in large excess. The higher proportion of methylation occurs with di-*n*-propyl disulphide, *i.e.*, with the least volatile substrate.

No allowance was made, however, for possible solubility of the mercury derivatives in the cyanide and chloride solutions. It is hoped to determine the ratio mercaptan : methyl alkyl sulphide more accurately. Methylation of ethyl and *n*-propyl mercaptans when added to the mould cultures (see p. 874) is also very incomplete.

It appears probable, therefore, that mercaptan formation is independent of and precedes methylation. The formation of mercaptan does not necessarily, however, involve a preliminary reduction, thus: $R_2S_2 + 2H = 2R{\cdot}SH$. Mercaptan may arise by hydrolytic fission: $R_2S_2 + H{\cdot}OH = R{\cdot}SH + R{\cdot}S{\cdot}OH$.

Important results have been obtained by Schöberl and his co-workers (*Annalen*, 1933, **507**, 111; 1936, **522**, 97) in an examination of the hydrolysis, in alkaline or neutral solution, of a large number of carboxylic acids containing the disulphide link. They have shown that the sulphenic acid, R·S·OH, breaks down to hydrogen sulphide and an aldehydo- or keto-acid; thus dithiodiglycollic acid, $(CO_2H{\cdot}CH_2{\cdot}S)_2$, gives thioglycollic and glyoxylic acids; disulphidosuccinic acid, $[CO_2H{\cdot}CH_2{\cdot}CH(CO_2H){\cdot}S]_2$, gives thiolactic and pyruvic acids. Hydrogen sulphide is obtained in each case. Reactions of this type are involved in the alkaline desulphurisation of cystine and the action of alkali on wool (Crowder and Harris, *J. Res. Nat. Bureau Standards*, 1936, **16**, 475).

This decomposition of the unstable intermediate sulphenic acids, giving aldehyde or ketone and hydrogen sulphide, is probably of the same type as that of the sulphoxides in presence of hydrochloric acid, which was described almost simultaneously by Smythe (J., 1909, **95**, 349) and by Pummerer (*Ber.*, 1909, **42**, 2283), and further studied by Larsson and Jönsson (*Ber.*, 1934, **67**, 1263) and by Hellström and Lauritzson (*Ber.*, 1936, **69**, 2003):

$$R{\cdot}CH_2{\cdot}SO{\cdot}CH_2R = R{\cdot}CHO + R{\cdot}CH_2{\cdot}SH$$

If the sulphenic acid as well as the sulphoxide be assumed to react in a tautomeric form, the analogy is readily seen:

$$R{\cdot}CH_2{\cdot}SO{\cdot}CH_2R \longrightarrow R{\cdot}CH{:}S(OH){\cdot}CH_2R \longrightarrow R{\cdot}CHO + R{\cdot}CH_2{\cdot}SH$$
$$R{\cdot}CH_2{\cdot}S{\cdot}OH \longrightarrow R{\cdot}CH{:}S(OH)H \longrightarrow R{\cdot}CHO + H{\cdot}SH$$

This reaction does not appear, however, to have been demonstrated in the case of the

simple dialkyl disulphides. Price and Twiss (J., 1910, **97**, 1183) showed that diethyl disulphide is completely decomposed at 150—180° by alcoholic potash, but only partly so on boiling under reflux. The products were not identified.

Mr. B. Taylor has recently shown that when diethyl disulphide is heated with water in a copper autoclave at 200—210° for four hours, extensive decomposition takes place. The aqueous liquor contained acetaldehyde, which was isolated as the 2 : 4-dinitrophenylhydrazone. The autoclave was coated with a mixture of copper sulphide and copper ethyl mercaptide, $Cu(SEt)_2$. This gave hydrogen sulphide and ethyl mercaptan on decomposition with acid, which were identified as lead sulphide and chloromercury ethylthiol mercurichloride, m. p. and mixed m. p. 150—151° with an authentic specimen of m. p. 151°. When heated in nitrogen, the deposit in the autoclave evolved ethyl sulphide : $Cu(SEt)_2 = CuS + Et_2S$. The ethyl sulphide was identified as the dimercurichloride, m. p. and mixed m. p. 117—118° with an authentic specimen of the same m. p.

The same decomposition, though less extensive, was observed on heating the disulphide and water in a sealed tube at 170° for 5 hours. Hydrolytic fission of the –S–S– group in diethyl disulphide is therefore possible; it is not yet clear whether this change can be effected under the conditions obtaining in the mould cultures. No acetaldehyde could be detected on passing the volatile products from bread cultures containing diethyl disulphide through a solution of 2 : 4-dinitrophenylhydrazine in dilute hydrochloric acid. The minute amount of precipitate produced did not suffice for a determination of m. p.

The methylation of mercaptans described in this paper may be explained on the assumption that formaldehyde (probably arising from glycine; see *Biochem. J.*, 1935, **29**, 1761; *Chem. and Ind.*, 1936, **55**, 900) condenses to form compounds of the type $R{\cdot}S{\cdot}CH_2{\cdot}OH$, which then undergo reduction. Such compounds have been described by Levi (*Gazzetta*, 1932, **62**, 775). The product from formaldehyde and ethyl mercaptan is very unstable and we could not obtain it free from the odour of mercaptan. Consequently the capacity of *P. brevicaule* to effect the change $Et{\cdot}S{\cdot}CH_2{\cdot}OH \longrightarrow Et{\cdot}S{\cdot}CH_3$ could not be tested, but the possibility of this type of biological reduction will be explored by the use of more stable compounds.

The discovery of djenkolic acid in the djenkol bean of Java (van Veen and Hyman, *Rec. trav. chim.*, 1935, **54**, 493; du Vigneaud and Patterson, *J. Biol. Chem.*, 1936, **114**, 533) lends further support to the formaldehyde theory of the methylation of mercaptans, as its constitution, $CH_2[S{\cdot}CH_2{\cdot}CH(NH_2){\cdot}CO_2H]_2$, shows it to be derived from formaldehyde and cysteine.

EXPERIMENTAL.

Preparation of Reference Compounds.—Methyl ethyl sulphide dimercurichloride. The sulphide (1·26 g.) was added to saturated aqueous mercuric chloride (300 c.c.). The white solid, which separated immediately, was removed next day, m. p. 124—126°. Two crystallisations from acetone gave a product of constant m. p. 127—128° (Found : C, 5·9; H, 1·6; S, 4·8; Cl, 22·7; Hg, 64·6. $C_3H_8S,2HgCl_2$ requires C, 5·8; H, 1·3; S, 5·2; Cl, 22·9; Hg, 64·8%). The *dimercurichloride* was also obtained, m. p. 126—127°, when the precipitate (m. p. 101°) resulting from the interaction of the sulphide (0·84 g., 1 mol.) and mercuric chloride (2·99 g., 1 mol.) in water (75 c.c.) was recrystallised twice from acetone. A pure monomercurichloride could not be isolated (compare Thierry, J., 1925, **127**, 2756, who obtained methyl ethyl sulphide from petroleum as the mercurichloride, which formed " rather unstable crystals," m. p. 101—102°).

Benzylmethylethylsulphonium picrate. Methyl ethyl sulphide (2·1 g.) was mixed with benzyl chloride (7 g.) in alcohol (15 c.c.). After several days water (20 c.c.) was added, and unchanged benzyl chloride removed by ether. Owing to the instability of sulphonium salts the solution was not concentrated but was treated with sodium picrate, and the resulting precipitate (m. p. 99—100°) recrystallised twice from alcohol (m. p. 100·5—101°) (Found : C, 48·3; H, 4·5; N, 10·9; picric acid, 58·1. Calc. for $C_{16}H_{17}O_7N_3S$: C, 48·6; H, 4·3; N, 10·6; picric acid, 58·0%).

Methyl n-*propyl sulphide mercurichloride.* The sulphide (0·5 c.c.) was shaken with an excess of saturated aqueous mercuric chloride, and the precipitate, m. p. 162—164°, recrystallised twice from benzene; it then had the constant m. p. 163·5—165°. Ingold, Jessop, Kuriyan, and Mandour (J., 1933, 533) record the m. p. 164—166°, but give no analysis (Found : C, 6·7; H, 1·2; S, 4·11; Hg, 64·7. Calc. for $C_4H_{10}S,2HgCl_2$: C, 7·6; H, 1·6; S, 5·1; Hg, 63·4%. Calc. for

$2C_4H_{10}S,5HgCl_2$: C, 6·2; H, 1·4; S, 4·2; Hg, 65·1%). A mercurichloride of the same m. p. and mixed m. p. and giving almost identical analyses was obtained from methyl *n*-propyl sulphide of biological origin (p. 875).

Benzylmethyl-n-*propylsulphonium picrate.* The sulphide (1 c.c.), benzyl chloride (5 c.c.), and alcohol (10 c.c.) were left for several days and diluted with water; after conversion into picrate without concentration, the crude product had m. p. 92—94° and 95—95·5° on recrystallisation from alcohol (Found: C, 49·9; H, 4·7; N, 10·4; picric acid, 55·8. Calc. for $C_{17}H_{19}O_7N_3S$: C, 49·9; H, 4·7; N, 10·3; picric acid, 56·0%).

Diethyl Disulphide and Mercuric Chloride.—When the disulphide (b. p. 153° after careful fractionation) and aqueous mercuric chloride were mixed in the molecular proportion 1 : 4 (A), or when the mercuric chloride was employed in excess (B), a white precipitate formed rather slowly. This melted at 151° and was insoluble in all the usual organic solvents. The same compound, m. p. 150° and mixed m. p. 151°, was obtained when ethyl mercaptan was added to an excess of saturated aqueous mercuric chloride (C). With hydrochloric acid it gave ethyl mercaptan. Sodium hydroxide gave yellow mercuric oxide but no odour of sulphide; no disulphide or mercaptan was obtained either in the cold or on warming. In an attempt to find a solvent for (A), about 0·1 g. was boiled with water (40 c.c.). The extract contained mercuric chloride, which suggested the presence of some loosely combined, probably co-ordinated, mercuric chloride in (A), (B), and (C). The residue (D) was then found to be unmelted at 260°, and still contained mercury and sulphur. With hydrochloric acid ethyl mercaptan was at once evolved.

The loss in weight on boiling (A) with three successive quantities of water and the mercury thus removed were determined and the insoluble residue (D) analysed [Found for (A): C, 4·7; H, 1·4; Hg, 70·2, 70·25; loss in weight on extraction with water, 48·1, 47·9; Hg removed as $HgCl_2$, 35·6, 35·75. Calc. for $C_2H_5S{\cdot}HgCl,HgCl_2$: C, 4·2; H, 0·9; Hg, 70·55; loss in weight, 47·8; Hg removable as $HgCl_2$, 35·3%. Found for (D): Hg, 67·2, 67·8. Calc. for $C_2H_5S{\cdot}HgCl$: Hg, 67·5%]. Analyses of the products obtained from di-*n*-propyl disulphide with mercuric chloride were effected in a similar manner (see below).

Two preparations of (A) were carried out in which 12·05 and 11·95 g. of diethyl disulphide were treated with mercuric chloride (108 g.; 4 mols.) in water (2 l.). After 15 days, during which the bottles were frequently shaken, the yields of (A) were 79·1 and 78·3 g. No further deposit separated from the filtrate. These figures represent yields of 94% and 95% of the amounts required by the summarised equation on p. 869.

Di-n-*propyl Disulphide and Mercuric Chloride.*—Di-*n*-propyl disulphide was prepared by heating sulphur (5·3 g., 1 atom) and sodium sulphide (13 g., 1 mol.) in *n*-propyl alcohol (150 c.c.) till amost complete solution occurred. *n*-Propyl bromide (41 g., 2 mols.) was then added, and the mixture refluxed for 4 hours. The mixture was poured into water (500 c.c.) and repeatedly extracted with ether, the solvent removed, and the residue fractionated at 16 mm. A small fraction, b. p. 80° (di-*n*-propyl sulphide boils at 141·5—142·5°), and one, b. p. 129°, were obtained, together with a fraction, b. p. 100—102°, which was pure di-*n*-propyl disulphide. Spring and Legros (*Ber.*, 1882, **15**, 1939), who prepared it from sodium *n*-propylthiosulphate, give b. p. 192·5° at ordinary pressure. In our preparation the presence of the fraction b. p. 129° (presumably a polysulphide) caused decomposition on distillation of the reaction product at ordinary pressure.

The disulphide (0·9 g.) and 3% aqueous mercuric chloride (300 c.c.) were frequently shaken during 4 days, giving 3·9 g. of a white solid (E), m. p. 139°. 0·68 G. of this product was treated with an excess of cold aqueous sodium hydroxide in a stream of air, which was passed through aqueous mercuric cyanide into 3% aqueous mercuric chloride. No deposit formed in either solution during 2 hours or throughout a further 3 hours during which the mixture was heated at 100°. The mixture was then acidified with hydrochloric acid, liberating *n*-propyl mercaptan, and aspiration continued into mercuric chloride; 0·60 g. of the original compound of m. p. 139° was then re-formed (F).

When (E) (0·5 g.) was boiled with water (100 c.c.) for 6 hours, the aqueous extract contained mercuric chloride. The insoluble residue (G) after washing melted at 182°. It gave a strong odour of a mercaptan with hydrochloric acid [Found for (E): C, 6·65; H, 1·4; S, 5·8; Hg, 68·6, 68·5; loss in weight on extraction with water, 47·0; 47·1; Hg removed as $HgCl_2$, 33·9, 34·1. Calc. for $C_3H_7S{\cdot}HgCl,HgCl_2$: C, 6·2; H, 1·2; S, 5·5; Hg, 68·9; loss in weight, 46·6; Hg removable as $HgCl_2$, 34·4%. Found for (G): C, 11·55; H, 2·3; S, 10·5; Hg, 64·7. Calc. for C_3H_7ClSHg: C, 11·55; H, 2·25; S, 10·3; Hg, 64·5%].

Ethyl Mercaptan and Mercuric Chloride.—Mercuric chloride (3 g.) in water (80 c.c.) was added to the mercaptan (2 g., 3 mols.). A red precipitate was immediately formed, quickly becoming pink and finally white. Next day the solid (m. p. 73°) was separated and after one

crystallisation from alcohol had m. p. 76—77° alone and in admixture with authentic mercury diethyl mercaptide.

Mercuric chloride (1·6 g.) in water (30 c.c.) was then added to the original filtrate, giving a white solid, m. p. 86°. Extraction of this with alcohol left a residue of ethylthiol mercury chloride, Et·S·HgCl, unmelted at 260°. The alcohol deposited a further quantity of the mercaptide, m. p. 76—77°.

Final addition of excess of aqueous mercuric chloride to the second main filtrate, which still contained mercaptan, gave a solid, m. p. 149° alone and 150° in admixture with the double compound Et·S·HgCl,$HgCl_2$, m. p. 151°, obtained from diethyl disulphide and mercuric chloride.

Later work showed that the ethyl mercaptan used in this experiment must have contained traces of hydrogen sulphide. A specimen which gave a clean yellow precipitate of lead ethyl mercaptide with lead acetate gave no red precipitate with mercuric chloride. If, however, a few bubbles of hydrogen sulphide were passed through the mercaptan, addition of mercuric chloride then gave a red solid, which became almost white on shaking with excess of the mercury salt.

This red solid is presumably identical with or related to the red compound $Hg(SEt)_2$,2HgS prepared by Sachs and Balassa (*Z. anorg. Chem.*, 1925, **145**, 196), who also describe a yellow isomer (see below). The excess of mercuric chloride probably removes the mercuric sulphide as the double compound $HgCl_2$,2HgS (Jolibois and Bouvier, *Compt. rend.*, 1920, **170**, 1497).

n-*Propyl Mercaptan and Mercuric Chloride.*—The mercaptan (Ingold *et al.*, *loc. cit.*) (0·5 c.c.) was mixed with an excess of saturated aqueous mercuric chloride and left overnight. The product had m. p. 138—139° (decomp.) alone and in admixture with (E) (m. p. 139° decomp.) and was therefore C_3H_7S·HgCl,$HgCl_2$. Mercuric chloride (2 g., 1 mol.) in water (80 c.c.) was added to the mercaptan (1·5 g., 3 mols.). The resulting white solid was separated next day and found to sinter from 60° to 120°. 0·5 G. was refluxed with alcohol (20 c.c.) for 30 minutes; the filtered solution deposited mercury di-*n*-propyl mercaptide, m. p. and mixed m. p. 65—66° with a specimen obtained from the mercaptan and mercuric cyanide. The residue insoluble in alcohol had m. p. 182° alone and in admixture with authentic *n*-propylthiol mercury chloride, C_3H_7S·HgCl (see p. 872).

The mercaptan (0·5 g.) was added to mercuric chloride (1·8 g., 1 mol.) in alcohol (60 c.c.), the mixture left overnight, and the solid then separated. It consisted of the thiol mercury chloride C_3H_7·S·HgCl and had m. p. and mixed m. p. 182°.

P. brevicaule Saccardo (*Baarn Strain* A; *see* J., 1933, 95) *and Diethyl Disulphide.*—Four 1 l. flasks each containing 150 g. of bread crumbs and 20—30 c.c. of water were sterilised, inoculated, and incubated for four days at 30°, and 1 day at room temperature. 25 C.c. of a sterile 2% aqueous suspension of diethyl disulphide were then added (final concentration in the bread, about 0·2%), and the flasks left for 1 day at room temperature. They were then connected in series (as described in Parts I—IV), and volatile products aspirated in a stream of sterile air through two bottles containing 4% aqueous mercuric cyanide, and then through five bottles containing 3% aqueous mercuric chloride. Four separate experiments, each with four bread flasks, were carried out, and in every case the precipitate of mercury diethyl mercaptide was confined to the first mercuric cyanide bottle. The observed m. p. varied from 71° to 74° and in one case a m. p. of 70—73° was obtained. The precipitates were often slightly yellowish-green. On recrystallisation from ethyl alcohol, only traces remained insoluble and the solution deposited the pure white mercury diethyl mercaptide $(C_2H_5{\cdot}S)_2Hg$, m. p. 76—77° (Found: C, 14·85; H, 2·8. Calc.: C, 14·9; H, 3·1%).

The yellow colour was probably due to a small amount of the yellow compound $Hg(S{\cdot}C_2H_5)_2$,2HgS (Sachs and Balassa, *Z. anorg. Chem.*, 1925, **145**, 196) arising from the presence of a trace of hydrogen sulphide. The amount was, however, too small to be cited as evidence of the formation of hydrogen sulphide by hydrolytic fission (see p. 870). The specimen of diethyl disulphide had been well fractionated after purchase, but may have contained a slight trace of hydrogen sulphide. In later experiments the disulphide was washed with dilute sodium hydroxide solution before fractionation and addition to the mould cultures. The mercury diethyl mercaptide produced was then quite white. Similar yellow precipitates were obtained by Rübner (*Arch. Hygiene*, 1893, **19**, 136) when methyl mercaptan containing hydrogen sulphide was passed into mercuric cyanide.

At the commencement of the experiment the m. p. of the deposit in the first mercuric chloride bottle is always below that (151°) of the pure compound C_2H_5·S·HgCl,$HgCl_2$ (A), and it falls as the experiment proceeds. This is due to the admixture of (A) with the dimercurichloride of methyl ethyl sulphide (m. p. 127—128°). This monosulphide reacts rapidly with mercuric chloride and is mostly retained in the first bottle. The disulphide, on the other hand, reacts more slowly and

tends to pass over into the second and third bottles. At any given time with very few exceptions the m. p. of the deposit in the second absorption bottle is found to be higher than that in the first, due to the predominance of (A). Later on, methylation ceases and as unchanged disulphide is still present, the m. p. of the deposits rises again to that of (A). Almost at the same time the deposition of mercaptide in the mercuric cyanide bottle ceases. As ethyl mercaptan is probably the precursor of methyl ethyl sulphide (see p. 870), this simultaneous cessation of reduction and methylation would naturally be expected. It is not clear, however, why reduction (or possibly hydrolysis; see p. 870) should cease while diethyl disulphide is still available.

Detection of Methyl Ethyl Sulphide in the Precipitate from the Mercuric Chloride Absorption Bottles.—(1) *As dimercurichloride.* The deposits having the lowest m. p.'s were collected, and 1·2 g. treated with cold sodium hydroxide solution. The odour of an alkyl monosulphide was at once apparent. A slow stream of air was then passed through the mixture into (a) aqueous mercuric cyanide (4%) and (b) aqueous mercuric chloride (3%). No deposit formed in (a) throughout the experiment, but after 30 minutes a precipitate formed in (b), the first mercuric chloride bottle. Two such deposits were removed and the reaction flask was then heated, giving a third deposit. All these had m. p. 126—127° and when mixed and recrystallised from benzene melted at 127—128° alone and in admixture with authentic methyl ethyl sulphide dimercurichloride, m. p. 127—128° (Found : C, 6·05; H, 1·65; Cl, 23·1; S, 5·0. Calc. for $C_3H_8S,2HgCl_2$: C, 5·8; H, 1·3; Cl, 22·9; S, 5·2%).

(2) *As benzylmethylethylsulphonium picrate.* A further 1·19 g. of the crude deposit were decomposed with sodium hydroxide solution as before, and the evolved sulphide aspirated through mercuric cyanide (no precipitate) into 5% alcoholic benzyl chloride (15 c.c.) during 36 hours. Addition of the minimum of water and extraction with ether left a solution, which with sodium picrate gave a precipitate, m. p. 97—99°. Three recrystallisations from alcohol gave benzylmethylethylsulphonium picrate, m. p. and mixed m. p. 100·5—101° with an authentic specimen of m. p. 100·5—101° (Found : C, 48·2; H, 4·35; N, 10·85. Calc. for $C_{16}H_{17}O_7N_3S$: C, 48·6; H, 4·3; N, 10·6%).

(3) *As methyl ethyl sulphide platinochloride.* A further 1·28 g. of the crude mercurichlorides from the absorption bottles were mixed with sodium hydroxide solution and shaken with three successive quantities of ether. The combined extracts were then shaken with aqueous potassium platinochloride for 18 hours, separated, and evaporated. The oily residue solidified and after two crystallisations from alcohol melted at 121·5—122·5° alone and in admixture with synthetic methyl ethyl sulphide platinochloride, m. p. 124—125° (Mann, J., 1930, 1745). The α- and β-modifications of the platinochloride of diethyl sulphide both melt at 108° (Klason, *Ber.*, 1895, 28, 1494).

Control experiment. To each of four 1 l. flasks containing sterilised but uninoculated bread were added 25 c.c. of a sterile 2% aqueous suspension of diethyl disulphide, and aspiration commenced as usual. No precipitate formed in the mercuric cyanide during 17 days. Fourteen deposits were taken from the mercuric chloride bottles, five of m. p. 151°, seven of m. p. 150°, and two of m. p. 149°. In order to confirm that no methylation had occurred the entire product was made alkaline with potassium hydroxide. Aspiration for 24 hours gave no precipitate in either the mercuric cyanide or chloride absorption bottles, indicating the complete absence of any alkyl monosulphide. The non-formation of mercaptan on treatment with alkali confirms the result obtained with precipitate (A) (p. 872).

P. brevicaule Saccardo *and Ethyl Mercaptan.*—Four 1 l. flasks of sterile bread were inoculated, incubated as usual, and treated with 25 c.c. of 2% aqueous suspension of ethyl mercaptan. The products were aspirated through mercuric cyanide (5 bottles) and chloride (3 bottles) as before. After 11 days the deposits in the first two cyanide bottles had m. p. 71—72° and in the corresponding chloride bottles 132° and 140°; the higher m. p. of the deposit in the second bottle was to be expected (p. 873). It is clear from these m. p.'s that some disulphide had been formed from the mercaptan during aeration. After a further 13 days the deposits in the first cyanide and the first chloride bottle had m.p. 71—72° and 150° respectively. The mercury diethyl mercaptide was recrystallised from alcohol, m. p. 76—77°. The mercurichlorides were collected and treated with alkali, and volatile matter aspirated through mercuric cyanide (no deposit) into mercuric chloride, giving a product, m. p. 126—127° alone and in admixture with authentic methyl ethyl sulphide dimercurichloride, m. p. 127—128°. There was insufficient for recrystallisation (Found : C, 6·0; H, 1·3; S, 4·7. Calc. for $C_3H_8S,2HgCl_2$: C, 5·8; H, 1·3; S, 5·2%).

P. brevicaule Saccardo *and Di-*n*-propyl Disulphide.*—The conditions in these experiments as regards number of culture flasks, weight of bread, concentration of added disulphide and absorption solutions were the same as for diethyl disulphide. The deposit from the mercuric cyanide

(0·4 g.) was crystallised once from alcohol, giving mercury di-*n*-propyl mercaptide, m. p. and mixed m. p. 65—66° with an authentic specimen, m. p. 65—66° (Found: C, 20·8; H, 4·3; S, 18·6. Calc. for $C_6H_{14}S_2Hg$: C, 20·6; H, 4·0; S, 18·35%).

Methyl n-*propyl sulphide mercurichloride.* The crude mercurichloride (0·3 g., m. p. 158—162°) obtained directly by absorption of the mould gases from di-*n*-propyl disulphide in mercuric chloride was recrystallised twice from alcohol; m. p. 163—164° [Found: C, 6·5; H, 1·2; S, 4·1; Cl, 22·3. Calc. for $C_3H_7{\cdot}S{\cdot}CH_3,2HgCl_2$: C, 7·6; H, 1·6; S, 5·1; Cl, 22·4%. Calc. for $2(C_3H_7{\cdot}S{\cdot}CH_3),5HgCl_2$: C, 6·2; H, 1·4; S, 4·2; Cl, 23·12%].

From the m. p. it would appear that this crude mercurichloride consisted almost entirely of methyl *n*-propyl sulphide mercurichloride, m. p. 163·5—165°, this being probably due to the relative non-volatility of di-*n*-propyl disulphide. The analytical results after recrystallisation moreover agree with those obtained for the synthetic product (see p. 872). Nevertheless in view of the somewhat unusual composition further purification was attempted by treatment of 0·86 g. with cold aqueous potassium hydroxide. Aspiration through mercuric cyanide gave no precipitate, but with mercuric chloride two deposits, both of m. p. 163°, were obtained. These were united and crystallised from benzene, giving a product of constant m. p. 163·5—165° alone and in admixture with a synthetic specimen. The analytical results were the same as before (Found: C, 6·6; H, 1·3; S, 4·0%).

Benzylmethyl-n-*propylsulphonium picrate.* The mercurichloride (m. p. 163—164°; 0·66 g.) from the absorption bottles was treated with cold sodium hydroxide solution, and the volatile sulphide aspirated through mercuric cyanide (no deposit) into alcoholic benzyl chloride during 48 hours. Conversion into picrate as before gave a solid, m. p. 91—93°, which, on recrystallisation from alcohol, gave benzylmethyl-*n*-propylsulphonium picrate, m. p. 95—95·5° alone or in admixture with an authentic specimen, m. p. 95—95·5° (Found: C, 49·3; H, 4·8; picric acid, 56·3. Calc. for $C_{17}H_{19}O_7N_3S$: C, 49·9; H, 4·7; picric acid, 56·0%).

P. brevicaule Saccardo *and* n-*Propyl Mercaptan.*—The experimental details were identical with those employed in the case of ethyl mercaptan. A precipitate quickly formed in the mercuric cyanide and, after about 12 hours, in the chloride solution. After 3 days these were removed (mercury di-*n*-propyl mercaptide: 2·84 g., m. p. 62—64°; 0·10 g., m. p. 160—162° respectively). The mercurichloride after two crystallisations from alcohol had m. p. 163—165° alone and 163·5—165° in admixture with synthetic methyl *n*-propyl sulphide mercurichloride (see above and p. 871). During the next 7 days 0·2 g. of mercaptide and less than 0·05 g. of product, m. p. 159—161°, formed in the cyanide and chloride bottles. No further deposits were obtained.

P. brevicaule Saccardo *and Diethyl Sulphide.*—The sulphide (25 c.c. of a 2% aqueous suspension) was added to each of four bread cultures of the mould, and volatile products aspirated as usual through mercuric cyanide and chloride. No deposit formed in the cyanide bottles during 14 days, by which time no further precipitate formed in the chloride. Several deposits were removed and each had m. p. 113—115°, which rose to 118° after one crystallisation from alcohol. Diethyl sulphide dimercurichloride prepared for comparison melted at 118—119°. The mould, as was to be expected, has no reducing action on diethyl sulphide.

P. brevicaule Saccardo *with Dibenzyl Disulphide and Diphenyl Disulphide.*—Small flasks containing 50 g. of sterile bread were inoculated and incubated as usual and treated with (a) 10 c.c. of 3% dibenzyl disulphide and (b) 10 c.c. of 2% diphenyl disulphide, both in aqueous suspension. No odour was observed during 30 and 35 days respectively. In the case of diphenyl disulphide four 1-l. flasks of bread cultures were set up, each treated with 25 c.c. of a 2% aqueous suspension, and volatile products aspirated through mercuric cyanide and chloride for 15 days. No precipitate formed in either case. Similar negative results have been obtained with phenylarsonic acid (Challenger and Rawlings, J., 1936, 264) and with benzylarsonic acid (Taylor, unpublished observation).

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182. *Liquid-phase Reactions at High Pressures. Part I. Hydrolysis of Esters, and the Knoevenagel Reaction.*

By D. M. Newitt, R. P. Linstead, R. H. Sapiro, and E. J. Boorman.

Foreword by William A. Bone and Jocelyn F. Thorpe.

The investigations embodied in this paper originated in representations made by us conjointly to the Research Council of Imperial Chemical Industries during 1932—33 to the effect that, having regard to the properties of high-tensile alloy steels available, no difficulty should be encountered in making and installing a complete laboratory apparatus for the explorative study of the effects of pressures up to 20,000 atmospheres upon organic chemical reactions in the liquid phase, according to a scheme submitted.

Eventually, in July, 1933, it was arranged that such an investigation should be undertaken, under grants from Imperial Chemical Industries Ltd., in the High Pressure Research Laboratories at the Imperial College, London, on the understanding that while Professor Thorpe, with Dr. Linstead, would be responsible for the organic chemical aspects of the work, Professor Bone, with Dr. D. M. Newitt, would be responsible for the high-pressure side of it.

Accordingly, an apparatus for pressures up to 5000 atm. was installed for the purpose, and work with it was begun in January, 1934, a further apparatus for pressures up to 20,000 atm. being added about a year later.

In recent years the effect of pressures of 3000 atm. and more on certain specific chemical reactions in the liquid phase have been investigated by Cohen, Bridgman, Conant, Tammann and others, and a more general survey has been made by Fawcett, Gibson and their collaborators (*J.*, 1934, 386, 396; *Proc. Roy. Soc.*, 1935, *A*, **150**, 223; 1936, **154**, 684). Earlier work is summarised in the first of these references.

We commenced by exploring a considerable number of reactions with the object of discovering those which showed large responses to pressures of the order of 5000 atm. No accurate quantitative measurements were attempted. The main positive responses were found in reactions of three classes :

(*a*) Hydrolysis of esters (and esterification of acids); (*b*) the Knoevenagel condensation and allied reactions; (*c*) polymerisation. The present paper deals with the investigation of the first two of these, the principal results being summarised below.

Hydrolysis and Esterification.—The system acetic acid + ethyl alcohol $\rightleftharpoons$ ethyl acetate + water is a classical example of a reversible bimolecular reaction, the equilibrium standing at about 66% esterification and being independent of temperature (Berthelot and St. Gilles, *Ann. Chim. Phys.*, 1862, **65**, 385; **66**, 1; **68**, 225). We found the same position of equilibrium at 5000 atm. pressure and 60°. It is of historical interest that Berthelot and St. Gilles observed no shift in equilibrium at a pressure of about 100 atm. (*loc. cit.*, **66**, p. 45). The constancy of this value is not surprising in view of the similarity between the molecular volumes of the two pairs of reactants. The effect of pressures of 500, 2000, 3500, 5000 and 6500 atm. on the velocity of this reaction at 60° in the absence of catalyst is shown in Table I and in Fig. 1. There is a large positive response. At 6500 atm. the system passes more than half way to equilibrium, under conditions which give a very small amount of esterification at atmospheric pressure. In Fig. 1 the percentage of acid esterified is plotted against log $(1000/t)$ for the various pressures, giving a series of approximately parallel lines. The approximate absolute velocity constants for the forward reaction were calculated, the value 4·0 being used for the equilibrium constant, and corrected for increase in concentration due to compressibility of the mixture. The values of k, in mols./l.-sec., are :

Pressure, atm.	1	500	2000	3500	5000	6500
$k \times 10^7$	3·031	4·256	11·87	29·85	76·9	168·2

We are endeavouring to obtain more precise information on this point.

Hydrolysis at room temperature. At 17° ethyl acetate was not appreciably hydrolysed by water at 5000 atm. pressure, but the hydrolysis by dilute mineral acid showed a positive response.

FIG. 1.

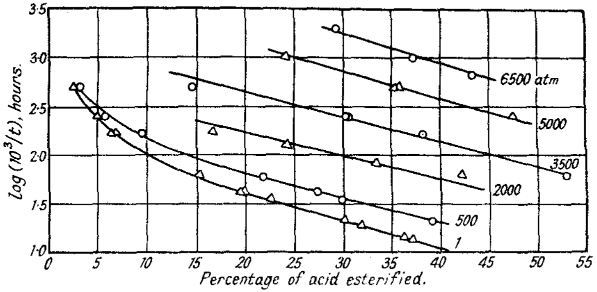


TABLE I.

Esterification of Equimolecular Mixtures of Acetic Acid and Ethyl Alcohol at 60°.

Time (hours).	Acid esterified, %, at (atmospheres). 1.	500.	2000.	3500.	5000.	6500.	Time (hours).	Acid esterified, %, at (atmospheres). 1.	500.	2000.	3500.
0·5	—	—	—	—	—	29·2	16	15·3	—	41·9	53·0
1·0	—	—	—	—	24·0	37·2	17	—	21·7	—	—
1·5	—	—	—	—	—	43·2	24	19·8	27·2	—	—
2	2·7	3·3	—	14·4	35·3, 35·8	—	28	22·3	—	—	—
3	—	—	—	—	46·5	—	29	—	29·8	—	—
4	4·8	5·7	—	30·2, 32·6	47·3	—	48	30·1	39·1	—	—
6	6·9	9·4	16·7	38·6	—	—	53	31·8	—	—	—
8	—	—	24·2	—	—	—	71	36·0	—	—	—
12	—	—	33·3	—	—	—	77	37·0	—	—	—

The ease of hydrolysis of many ethyl esters by water alone, or by dilute acids, was very strikingly increased by the application of pressure. For instance, ethyl oxalate, cyanoacetate, and chloroacetate, when in the pure state, were not appreciably hydrolysed by water at room temperature and atmospheric pressure during 3—4 days, although a very slow reaction could be detected later, catalysed by the acid formed. Under a pressure of 5000 atm. and at 17° ethyl oxalate was hydrolysed to the extent of 50% in a day, and the reaction was nearly complete in a week (see Table II). Apart from certain polymerisations observed by Conant and by Fawcett and Gibson, this seems to be the most striking positive effect so far achieved in liquid-phase reactions at high pressure. The pressure hydrolysis was doubtless facilitated by the separation of solid oxalic acid dihydrate which was observed during the later stages. The hydrolyses of ethyl chloroacetate, cyanoacetate, and trichloroacetate by water alone showed considerable although less marked responses to high pressure. Cyanoacetic acid cannot readily be isolated by the hydrolysis of its ester by the usual methods, but this can easily be achieved by hydrolysis with water alone or with dilute acid under a pressure of 5000 atm. The esterification of chloroacetic acid is also facilitated at high pressure.

Ethyl malonate was not hydrolysed at room temperature by water alone at 5000 atm. pressure, but hydrolysis by dilute solutions of hydrochloric or malonic acid was accelerated. The hydrolysis with mineral acid yielded a mixture of half ester and acid. Ethyl diethylmalonate behaved similarly. The hydrolysis by dilute acid of two typical natural mixtures of mixed glycerides represented by linseed oil and soya-bean oil showed a positive response

TABLE II.

Hydrolysis of Ethyl Esters at Room Temperature.

(3 Mols. of water per mol. of ester group were added in every case.)

Ester (1 mol.).	Mols. per ester group of EtOH.	Mols. per ester group of HCl.	Experimental conditions. Press., *P*, in atm.	Experimental conditions. Temp.	Experimental conditions. Time, hours.	Hydrolysis, %. At *P* atm.	Hydrolysis, %. At 1 atm.
Oxalate	[Sufficient for solution]	—	5000	16°	3	5	0·0
		—	5000	16	24	50	0·0
		—	5000	17	96	80	1·7
		—	5000	17	168	90	4·8
Acetate	0·75	—	5000	17	240	0·6	0·0
	0·75	0·025	5000	17	24	41·4	18·7
	0·75	0·025	5000	23	72	43·1	39·5
Malonate	1·5	—	5000	18	72	0·0	0·0
	1·5	0·025	5000	22	72	37·5	11·1
Succinate	1·5	—	5000	17	72	0·0	0·0
Ethylmalonate	1·5	0·025	5000	24	72	14·8	1·0
Cyanoacetate	1·5	—	5000	17	96	3·4	0·5
	1·5	—	5000	18	240	16·7	1·4
	1·5	0·005	5000	21	24	5·9	1·2
	1·5	0·025	5000	21	24	22·0	3·2
Chloroacetate	2·0	—	1000	21	72	0·5	0·3
	2·0	—	2050	21	72	1·8	0·3
	2·0	—	2900	19	72	3·7	0·3
	2·0	—	4000	18	72	7·2	0·3
	2·0	—	5000	18	72	14·8	0·3
Trichloroacetate	2·75	—	5000	23	72	48·9	15·3

to high pressure. The accelerated hydrolysis of fats by alkali under pressures of the order of 100 atm. is already known and forms the subject matter of patented processes. On the other hand, tristearin could not be hydrolysed by water, dilute acid, or dilute alkali at 5000 atm. and at room temperature; neither could positive indications be obtained of the hydrolysis of ethyl benzoate and ethyl succinate. The results are summarised in Table II.

Knoevenagel and Allied Reactions.—The reaction between cyanoacetic ester and various cyclic ketones was selected for study because some information was already available on the speed of the reaction at atmospheric pressure, and because the velocity could conveniently be altered by varying the amount of the catalyst, piperidine (Barrett and Linstead, *J.*, 1935, 436).

High pressures were found to have a very considerable effect on these condensations. In the presence of 0·05 mol. of piperidine, *cyclo*pentanone and cyanoacetic ester at atmospheric pressure and 18° yielded 3% of *cyclo*pentylidenecyanoacetic ester in 30 minutes. Under the same conditions of temperature and concentration but at 5000 atm. pressure the yield was 50%, and at 15,000 atm. the condensation was practically complete. The reaction was inconvenient, however, in that the reaction mixture solidified, and the containing tubes tended to fracture on release of the pressure. The analogous condensation with *cyclo*hexanone was free from this defect, and showed a similar response to the application of pressure (Table III). No condensation could be observed between *cyclo*hexanone and

TABLE III.

cyclo*Hexanone + Cyanoacetic Ester with and without Piperidine.*

Piperidine, mols.	Temp.	Press. (atm.).	Time (hours).	Yield of ethyl *cyclo*hexylidenecyanoacetate, % of theory. Under pressure.	Yield of ethyl *cyclo*hexylidenecyanoacetate, % of theory. At atmospheric pressure.
0·05	18°	4000	0·5	72	38·5
0·025	18	4000	0·5	65·5	20·6
—	18	4000	0·5	Nil	Nil
—	60	3200	50	11·7	,,
—	60	3200	124	13·2	,,
—	60	5000	80	26·3	,,

cyanoacetic ester at atmospheric pressure in the absence of a catalyst. It was therefore of great interest to find that these reagents yielded *cyclo*hexylidenecyanoacetic ester at 60°

and 5000 atm. pressure without the addition of piperidine. In view of the fact that *cyclo*hexanone failed to condense with either malonic or acetic ester under these conditions, it is possible that the nitrogenous group of either the original cyano-ester or the condensation product, acting in the imino-phase as a base, catalyses the high-pressure condensation.

It has been found that the Knoevenagel condensation is inhibited by substituents adjacent to the ketonic group (Barrett, Cook, and Linstead, J., 1935, 1065). Ethyl 2-methyl*cyclo*hexanone-2-carboxylate fails to react with cyanoacetic ester in the presence of piperidine at atmospheric pressure over long periods. We find that a small but definite degree of condensation occurs in the course of a few days at a pressure of 4000 atm. Dr. A. F. Millidge found the product to be ethyl 2-methyl*cyclo*hexylidene-1-cyanoacetate-2-carboxylate (J., 1936, 484). Ethyl 2-methyl*cyclo*hexanone-2-β-propionate, however, failed to react appreciably with cyanoacetic ester in the presence of piperidine even under a pressure of 5000 atm.

Although *cyclo*hexanone failed to condense with ethyl acetate in the presence of piperidine at high pressure, the reaction mixture afforded a poor yield of 2-Δ^1-*cyclo*hexanyl-*cyclo*hexanone (Wallach, *Ber.*, 1907, **40**, 70; Kon and Nutland, J., 1926, 3101), formed by condensation of two molecules of the ketone. The same condensation occurred in the absence of diluent, and also, to a slight extent, in the absence of catalyst. *cyclo*Pentanone condensed with itself in a similar manner at high pressure, but more readily (see Table IV). The product was 2-*cyclo*pentylidene*cyclo*pentanone, identical with that prepared by Wallach's method (*Ber.*, 1896, **29**, 2963). Self-condensation of ketones of this type in the presence of piperidine has not previously been observed, and we could detect no condensation in control experiments at atmospheric pressure.

TABLE IV.

Autocondensation of cyclo*Hexanone and of* cyclo*Pentanone under Pressure at* 60°.

Ketone.	Press., atm.	Time (hours).	Diluent (1 mol.).	Quantity of piperidine (mols.).	Yield of unsaturated ketone, % of theory.
$C_6H_{10}O$	4500	120	EtOAc	—	1·4
,,	4500	120	Ethyl malonate	—	2·0
,,	4500	120	EtOAc	0·05	9·0
C_5H_8O	4500	120	,,	0·05	40·0
$C_6H_{10}O$	4000	24	—	0·05	5
C_5H_8O	4000	24	—	0·05	45·5
,,	4000	22	EtOAc	0·1	(*a*) 45, (*b*) 45

Control experiments corresponding with all the above, under identical conditions but at atmospheric pressure, yielded no detectable amount of condensation product in any case.

Fawcett and Gibson's early results were generalised as follows: (1) That reactions which proceeded slowly at atmospheric pressure showed increased velocity at the same temperature under high pressure; and (2) that reactions which did not proceed at atmospheric pressure (in the absence of catalysts) did not proceed at pressures up to 3000 atm. Later work (*loc. cit.*, 1935—36), concerned with a more accurate study of certain reactions, did not affect these main conclusions.

Our results agree with (1), but we have found four reactions, mentioned above, which proceed at pressures of the order of 5000 atm. but are not detectable at atmospheric pressure under the same conditions. Fawcett and Gibson themselves observed an exception to (2) in the condensation and polymerisation of acetaldehyde (*loc. cit.*, 1934). It is obviously difficult in practice to decide whether a given reaction proceeds at atmospheric pressure with a very slow velocity or not at all. The hydrolyses of ethyl cyanoacetate and chloroacetate by water are examples of reactions, accelerated by high pressures, which are just detectable at ordinary temperature and pressure. In any case it is clear that, as a practical generalisation, it is no longer correct to say that liquid-phase reactions which do not proceed at atmospheric pressure also do not proceed at high pressures under otherwise like conditions.

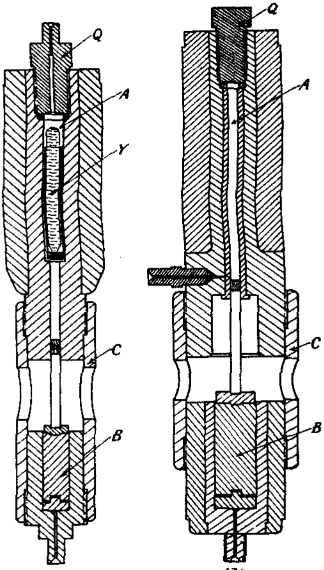
EXPERIMENTAL.

With the aid of modern high-tensile steels the production and maintenance of high pressures is no longer a matter of great difficulty; and provided suitable methods of construction are

adopted, reaction vessels of moderate size may be designed with a suitable factor of safety for pressures of 10,000 atm. and even higher (Newitt, *Trans. Inst. Chem. Eng.*, 1936).

In the work now described two such vessels have been employed capable of withstanding internal pressures of 5000 and 20,000 atm. severally. Both are cylindrical in shape and are built [see Figs. 2 (*a*) and 2 (*b*)] by shrinking together two or more steel tubes in such a way that the inner layers of the walls of the resulting compound cylinder are in compression and the outer layers in tension. The curves in Fig. 3 show the calculated distribution of hoop stresses in the walls of the 20,000-atm. vessel before and during the application of the working pressure. It should be noted that at maximum pressure the tensile hoop stresses nowhere exceed 40 tons per sq. inch, a figure providing a satisfactory margin of safety.

FIG. 2.



Each vessel consists of a reaction chamber *A* (Fig. 2) and an intensifier *B* connected by means of a steel sleeve *C*. The reactants are contained in a glass vessel *Y* [Fig. 2 (*a*)] inverted over mercury in a stainless-steel cup. The remaining free space in the reaction chamber is filled with liquid paraffin, which serves to transmit the pressure to the reactants as the pistons of the intensifier advance.

The method of carrying out an experiment is briefly as follows. The reactants are placed in the upper cylinder *A* (Fig. 4) of the intensifier, which is then filled with liquid paraffin and closed by the end-plug *Q*. By means of the hand pump *N*, a pressure of 1000 atm. is applied through the plug *Q*; the valve *V* is then closed, and pressure is slowly applied to the low-pressure side of the intensifier until the requisite experimental pressure, as measured by the free-piston pressure balance *B* and the gauge *G*, is obtained. Usually this part of the experiment occupies from 5 to 10 minutes, sufficient time being allowed to ensure that the compression is practically isothermal. When the reaction is to be carried out at a temperature above atmospheric, the

chamber is raised to the desired temperature, before introduction of the reactants, by means of an electric furnace, and the temperature is thus maintained throughout the experiment. The

FIG. 3.

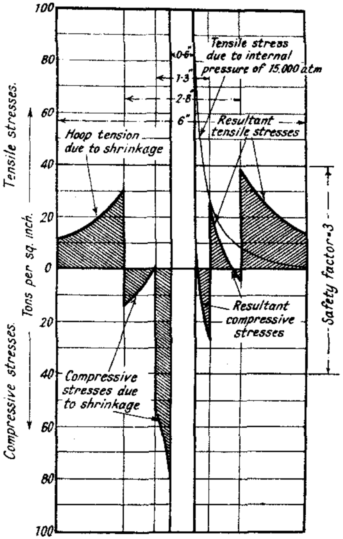
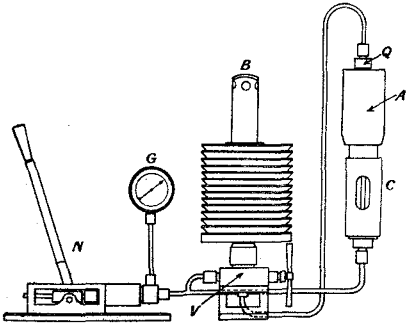


FIG. 4.



pressures indicated by *B* and *G* correspond with the ratios of the areas of the pistons of the intensifier, due allowance being made for frictional losses; it is therefore not essential always to employ the pressure balance provided the gauge *G* is calibrated at frequent intervals. In work-

ing at 15,000 atm., the intensifier was calibrated by the pressure balance up to 5000 atm. and by a manganin resistance gauge to the higher pressure.

Ethyl Acetate–Acetic Acid System.—A.R. Reagents were used. Aliquot portions of the pressure-treated sample were titrated with standard alcoholic potash. A known excess of the potash was then added, the samples were heated under reflux on a steam-bath for 15 minutes (soda-lime guard-tube), cooled, and the excess of alkali estimated with standard acid. In this way the acid and ester present were estimated. Trial experiments showed the method to be satisfactory. When mineral acid was used as catalyst in hydrolyses, an allowance was made in the first titration. The results are summarised in Table I, and the effect of high pressure upon the velocity is shown graphically in Fig. 1.

Experiments on the hydrolysis of ethyl acetate with an excess of water and with dilute acid are summarised in Table II. These show an approach to an equilibrium.

Hydrolysis of Ethyl Oxalate.—The ester was purified by standing over anhydrous potassium carbonate, and was distilled at 76°/11 mm. Analysis by the methods described below showed it to be free from acid. It was not possible to estimate the free acid in a hydrolysed portion by direct titration owing to the rapid hydrolysis of unchanged ester, and the following method was used. The liquid to be analysed was diluted with aqueous alcohol until 25 c.c. contained the equivalent of about 1 g. of ethyl oxalate. The total amount of ester + acid was then estimated by refluxing a 25-c.c. sample for an hour with a known excess of $N/2$-alcoholic potash and back-titrating with standard acid. A second 25-c.c. portion was shaken for 10 minutes with an excess of pure precipitated barium carbonate to neutralise the free acid. The remaining ester was estimated by hydrolysis as before. Separate experiments showed that the presence of the barium salts was not deleterious, and test analyses gave satisfactory results.

A mixture of 1 mol. of ethyl oxalate with 6 mols. of distilled water, and the minimum amount of absolute alcohol (freed from acidic impurities by distillation from quick-lime) needed for miscibility, was left at 17° in the dark. Portions removed at intervals were analysed :

Time (days)	4	7	10	21
Hydrolysis, %	1·7	4·8	9·2	33·0

No solid separated in these experiments. Similar experiments at 5000 atm. for 3 hours, 1, 4, and 7 days, under otherwise identical conditions, gave the results shown in Table II. A considerable amount of oxalic acid dihydrate (m. p. and mixed m. p. 102°) was formed in the two longest experiments.

Other Ester Hydrolyses.—These are summarised in Table II; the general procedure and analytical methods were those described above for ethyl acetate unless otherwise stated. A few supplementary notes are appended.

Ethyl malonate, free from nitrogenous material, was prepared by the esterification of malonic acid and had b. p. 96°/22 mm. The hydrolysis product obtained from this by the use of dilute hydrochloric acid for 3 days at 5000 atm. and 22° was separated semi-quantitatively by means of sodium bicarbonate into acid and neutral fractions. The proportions of acid and half-ester in the acid fraction were estimated approximately by titration with alcoholic potash. Expressed in terms of ester groups hydrolysed, the hydrolysis was 37·5%. The composition of the product was approximately: malonic acid, 19; ethyl malonate, 43; half-ester, 38%.

Ethyl cyanoacetate, purified by distillation, had b. p. 121°/46 mm., $n_D^{20^\circ}$ 1·4170, $d_{4^\circ}^{20^\circ}$ 1·0654. Hydrolysis with 3 mols. of water and 1·5 mols. of alcohol for 10 days at 18° and 5000 atm. proceeded to 16·7%. The product was separated into ester and acid by means of sodium bicarbonate. The ester was unchanged in physical properties, and there was no change of the cyano-group. The acid was pure cyanoacetic acid, m. p. and mixed m. p. 68°. The yield of this was 16%, corresponding with the figure obtained by titration. The product from the hydrolysis with $N/2$-hydrochloric acid at 5000 atm. (22% hydrolysis by titration) was separated similarly into pure cyanoacetic ester and acid (20% yield; m. p. 69°; equiv., 85·0; calc., 85·0).

Ethyl chloroacetate (Conrad, *Annalen*, 1877, **188**, 218) had b. p. 142°, $n_D^{20^\circ}$ 1·4205, $d_{4^\circ}^{20^\circ}$ 1·1498. For analyses of mixtures of acid and ester, the hydrolysis was carried out with $N/10$-aqueous baryta instead of alcoholic potash, to prevent removal of chlorine. Ten minutes' heating on the steam-bath was sufficient for hydrolysis. The product from the hydrolysis with water alone was separated into pure chloroacetic acid, m. p. and mixed m. p. 63°, equiv. 95·0 (calc., 94·5), and ester, b. p. 143°, $n_D^{20^\circ}$ 1·4202, $d_{4^\circ}^{20^\circ}$ 1·1486. No chloride ion could be detected.

A solution of 1 mol. of chloroacetic acid in 3 mols. of absolute alcohol was submitted to a pressure of 5000 atm. for 3 days at 19°. The ester was formed in 72·7% yield, and had pro-

perties almost identical with those given above. In a control experiment at atmospheric pressure, 26·4% of esterification occurred.

Ethyl trichloroacetate (Spiegel and Spiegel, *Ber.*, 1907, **40**, 1734) had b. p. 74°/28 mm. The mixtures of acid and ester could not be analysed by the methods given above, but the acid could be estimated by direct titration of a known weight of mixture with N/10-sodium carbonate (methyl-orange). The product of the pressure hydrolysis (48·9% acid) contained no chloride ion. Trichloroacetic acid (49%) was isolated by separation with sodium bicarbonate.

Ethyl benzoate was completely unaltered by water (10 days) and by dilute hydrochloric acid (7 days) at 18° and 5000 atm. pressure under the same general conditions.

Stearin, prepared from stearic acid by Joglekar and Watson's method (*J. Soc. Chem. Ind.*, 1928, **47**, 365), was made into a thick paste with 30 mols. of water and a small quantity of acetone as a wetting agent. There was no hydrolysis after 6 days at 5000 atm. pressure and 17°. Negative results were also obtained in similar experiments with N/10- and N/2-hydrochloric acid, and with dilute potash.

Linseed oil (5·9 g., alkali-refined) was dissolved in a mixture of 1·1 c.c. of 0·536N-hydrochloric acid, 5 c.c. of ether, and 21 c.c. of acetone. After 6 days at 16° and 5000 atm., there was 9·5% hydrolysis. A control experiment under atmospheric pressure showed 3·7% hydrolysis.

Analogous experiments with water in place of hydrochloric acid gave no hydrolysis either at 1 or at 5000 atm. pressure. Hydrolysis with dilute alkali appeared too rapid for convenient manipulation. Soya-bean oil, treated in exactly the same way as linseed oil, showed 11·2% hydrolysis at 5000 atm. and 2·2% at atmospheric pressure.

Knoevenagel and Other Condensations (see Tables III and IV).—The products were separated by fractional distillation under reduced pressure, and were identified as follows :

*cyclo*Pentylidenecyanoacetic ester : b. p. 180—182°/25 mm., m. p. 57—58° (crude), 58° after crystallisation from alcohol, mixed m. p. 58°.

*cyclo*Hexylidenecyanoacetic ester, from pressure experiments without piperidine : b. p. 150—160°/20 mm., m. p. — 2°, $n_D^{20°}$ 1·4960 (crude). Material made with piperidine at atmospheric pressure had b. p. 155—160°/20 mm., m. p. — 1°, $n_D^{20°}$ 1·4940, mixed m. p. — 2°.

2-Δ^1-*cyclo*Hexenyl*cyclo*hexanone, from pressure experiments without piperidine. The crude product, b. p. 143—145°/15 mm., was converted into semicarbazone, and the yield (Table IV) was calculated from the weight of this after drying. After washing with benzene and light petroleum, the semicarbazone melted at 192° alone or admixed with an authentic specimen, m. p. 192°. Kon and Nutland (*loc. cit.*) found that this ketone, b. p. 150°/18 mm., gave a semicarbazone, m. p. 194°, which could be separated by fractional crystallisation into two forms, m. p. 200° and 172°.

2-*cyclo*Pentylidene*cyclo*pentanone, from pressure experiments with piperidine : b. p. 130—140°/15 mm., $n_D^{18°}$ 1·5130; semicarbazone, m. p. 210—212° alone, 214—216° in admixture with an authentic specimen, m. p. 222°. Kon and Nutland found b. p. 135°/25 mm., $n_D^{19°}$ 1·5215, for the ketone. The yields of this ketone in Table IV are calculated from the weights of dry semicarbazone.

In conclusion we wish to thank Professors Bone and Thorpe, and Imperial Chemical Industries Limited for grants to defray the cost of the apparatus and for maintenance grants.

IMPERIAL COLLEGE, LONDON, S.W. 7. [*Received, April 5th*, 1937.]

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183. *The Crystalline Structure of the Sugars. Part IV. Pentaerythritol and the Hydroxyl Bond.*

By F. J. LLEWELLYN, E. G. COX, and T. H. GOODWIN.

ALTHOUGH it has been possible to make some progress toward the elucidation of the crystalline structure of the sugars by comparative studies of a large number of compounds (see, *e.g.*, Cox, Goodwin, and Wagstaff, J., 1935, 978, 1495), yet exact quantitative investigation of individual compounds has been hampered by lack of knowledge of various inter-atomic distances for preliminary " trial and error " determinations. No accurate measurements, so far as we are aware, had previously been made (on crystalline substances) either of the

length of the link from a carbon atom to an oxygen atom in an aliphatic alcohol, or of the length of the " hydroxyl bond " between two alcoholic groups, and indeed, direct measurements by Fourier analysis of the carbon–carbon bond in purely aliphatic compounds have been restricted to those made on oxalic acid and its derivatives, which are scarcely typical of aliphatic compounds in general. The " hydroxyl bond " in particular undoubtedly plays a very large part in determining the mutual arrangement of the molecules in crystalline sugars and alcohols, while many of the colloidal properties of the polysaccharides can be given satisfactory interpretation by postulating such a link. The present work on pentaerythritol, $C(CH_2{\cdot}OH)_4$, was undertaken in the hope that the relatively small number of parameters in the structure would permit precise determinations of this bond and of the carbon–oxygen distance. Additional interest attaches to pentaerythritol, since it was the centre of acute controversy some years ago owing to the supposed possibility of a pyramidal disposition of the valency bonds around the central carbon atom (see *e.g.*, " Strukturbericht," Vol. 1, p. 643; *Ann. Reports*, 1929, **26**, 74, 304). Our investigation, in addition to providing the data regarding inter-atomic distances for which it was primarily undertaken, has shown that the deviation of the central carbon valencies from the exact tetrahedral distribution is on the average no more than $1\frac{1}{2}°$, an amount very little more than the experimental error and which can easily be accounted for by inter-molecular forces.

Preliminary Crystallographic Data.—Our preliminary results confirmed those previously obtained, *viz.*, that pentaerythritol has a body-centred lattice of at least approximately tetragonal symmetry, with two molecules in the unit cell. The symmetry of pentaerythritol has been discussed at great length by earlier workers (for references, see " Strukturbericht," *loc. cit.*), and the final conclusion was that its space-group is $I\bar{4}$, so that the molecule possesses a four-fold alternating axis, a result which is compatible with the tetrahedral distribution of valencies about the central carbon atom. Since, however, both the measurement of cell dimensions and the intensity data available for the earlier discussions appeared to be limited in scope and accuracy, the possibility was still open that the substance was actually monoclinic–pseudo-tetragonal. Accordingly, experiments were made to determine whether any difference existed between the lengths of the two a-axes, and whether the angle between them departed appreciably from 90°. For this purpose a crystal was set up as for rotation about its tetragonal axis, and two successive oscillation photographs were taken on a cylindrical film surrounding it. The two oscillations were exactly 90° apart, and for the second one the film was displaced about 1 mm. parallel to the axis of rotation, so that each (hkl) reflection on the photograph was accompanied by the corresponding $(k\bar{h}l)$ reflection, any difference in the spacing being indicated by a *horizontal* separation of the two spots in addition to the vertical separation of 1 mm. On several such photographs no indication of any horizontal displacement was obtained, and examination of various pairs of planes with high indices showed that they differed in spacing by considerably less than half the separation of the $K\alpha$ doublet of copper, *i.e.*, by less than 0·05%. There is consequently no reason to doubt that the lattice of pentaerythritol is truly tetragonal; this is further confirmed by the observation that within the experimental error the intensities of the four planes (hkl) $(\bar{h}\bar{k}l)$, $(k\bar{h}\bar{l})$, $(\bar{k}h\bar{l})$, are always equal, while the alternating character of the symmetry is shown by the inequality (in general) of the intensities of the planes (hkl) and $(\bar{h}kl)$. These X-ray measurements appear to us to constitute a more searching test of the symmetry than goniometric or other external observations, and, coupled with the absence of reflections from planes for which $h + k + l$ is odd, they show that the space group is indeed $I\bar{4}$. The actual cell dimensions we find to be $a = 6{\cdot}10$, $c = 8{\cdot}73$ A. (each $\pm$ 0·02 A.), whence the calculated density for two molecules in the unit cell is 1·396 g./c.c. (observed, by flotation, 1·390 g./c.c.).

Measurement of Intensities.—In order to make the structure analysis as complete as possible, the intensities of all the reflections obtainable with copper $K\alpha$ radiation were measured, and in addition the $\{hk0\}$ intensities were determined to the limit attainable with molybdenum $K\alpha$ radiation. All the measurements were made photographically, and the intensities were put on the absolute scale by direct photometric comparison of the orders of {002}, {200}, and {101} with the (400) rock-salt reflection, extended faces and parallel-sided sections of known thickness being used. The remaining intensities were obtained from small

crystals completely bathed in the X-ray beam; the {$h0l$} and {$hk0$} reflections were measured by means of a Cambridge micro-photometer, and the {hkl} intensities were estimated visually by comparison with the {$h0l$} and {$hk0$} planes. Since the relatively high symmetry of the crystals enables each plane to be observed several times and compared with different standard reflections, visual comparison can be relied upon in this case to give absolute intensities with an accuracy adequate for the purposes of structure analysis ($\pm$ 20% or better for a plane of average intensity).

In Table I the data for the {$hk0$} planes are given; d is the spacing of the plane in A., and Q is the absolute integrated intensity from a crystal of unit volume (for $\lambda = 0{\cdot}710$ A.). The experimental structure factors $F_{\text{obs.}}$ are derived by means of the usual formula

$$Q = \frac{N^2e^4\lambda^3}{2m^2c^4} \cdot \frac{1 + \cos^2 2\theta}{\sin 2\theta} \cdot F^2$$

The values of $F_{\text{obs.}}$ for the other planes are given in Table II.

TABLE I.

hk0 *Structure Factors.*

$hk0$.	d.	$Q \times 10^4$.	$F_{\text{obs.}}$	$F_{\text{calc.}}$	$hk0$.	d.	$Q \times 10^4$.	$F_{\text{obs.}}$	$F_{\text{calc.}}$
200	3·08	11·80	37·2	−33·8	4100	0·57	<0·01	<3·3	5·0
400	1·54	0·20	5·3	1·3	510	1·19	0·90	14·8	12·9
600	1·03	0·11	5·8	5·4	530	1·05	0·03	3·2	4·5
800	0·76	0·04	4·2	4·0	550	0·86	0·02	3·1	− 1·0
1000	0·61	0·02	3·1	− 1·7	570	0·70	<0·01	<2·8	− 0·7
110	4·28	8·23	22·7	22·7	590	0·59	<0·01	<3·2	2·5
130	1·92	<0·06	<2·8	− 2·4	620	0·96	<0·02	<2·8	− 0·9
150	1·19	0·51	11·3	− 9·6	640	0·84	0·09	6·0	6·0
170	0·86	0·67	16·2	20·6	660	0·71	0·04	4·6	− 4·8
190	0·67	0·09	7·1	− 7·3	680	0·61	0·06	6·0	6·5
220	2·14	4·60	24·3	26·7	6100	0·52	0·01	3·2	0·2
240	1·36	0·25	3·7	− 5·9	710	0·86	0·12	6·9	− 8·8
260	0·96	0·07	4·9	5·8	730	0·81	<0·01	<2·8	1·2
280	0·73	0·01	2·6	5·1	750	0·70	<0·01	<2·8	2·7
2100	0·60	<0·01	<3·2	− 2·0	770	0·61	0·01	2·5	2·7
310	1·92	1·06	12·3	− 7·3	820	0·73	<0·01	<2·7	− 2·0
330	1·43	0·76	12·6	13·1	840	0·68	<0·01	<2·9	− 3·8
350	1·05	0·32	9·7	8·7	860	0·61	0·16	10·4	12·8
370	0·80	0·08	6·0	− 7·2	910	0·67	0·10	7·5	8·6
390	0·64	0·02	3·6	6·3	930	0·64	<0·01	<3·1	− 3·7
420	1·36	0·25	7·4	6·5	950	0·59	0·02	3·7	4·1
440	1·07	0·20	7·6	9·7	1020	0·60	0·04	5·2	4·4
460	0·84	<0·01	<2·5	− 1·2	1040	0·57	<0·01	<3·3	5·0
480	0·68	0·02	4·1	− 3·3	1060	0·52	<0·01	<3·5	− 5·0

Apart from the plane (002), the observed structure factors do not appear to suffer from serious errors due to extinction. Thus in the case of the very strong reflection (202), two values of $F_{\text{obs.}}$, obtained severally by reflection from a ground face and by transmission through a plate, were equal within experimental error (32·8 and 34·2), whereas appreciable extinction would have resulted in a higher value in the former case. Measurements which we have made on various planes in the crystals of β-methylxyloside also show that extinction effects are small, so that it is probable that in sugars, sugar alcohols, and similar substances whose molecules are held together mainly by hydroxyl bonds, the crystals approximate to the ideally imperfect type. In the case of the (002) reflection of pentaerythritol, however, extinction is very marked, the intensity from a cleavage face being increased several-fold by grinding and still more by immersion in liquid air. This is probably to be explained by the perfect cleavage parallel to (002) which would result in more perfect alinement of the mosaic blocks parallel to this plane than in other directions, added to which its outstandingly high intensity renders it more susceptible than any other to extinction effects.

The Determination of the Structure.—The unit cell of pentaerythritol contains two carbon atoms in the special positions (000) and ($\frac{1}{2}\frac{1}{2}\frac{1}{2}$), eight carbon atoms in the general positions $(x_1y_1z_1)$, $(\bar{x}_1\bar{y}_1z_1)$, $(y_1\bar{x}_1\bar{z}_1)$, $(\bar{y}_1x_1\bar{z}_1)$, $(\frac{1}{2}+x_1, \frac{1}{2}+y_1, \frac{1}{2}+z_1)$, etc., and eight oxygen atoms in the general positions $(x_2y_2z_2)$, etc. Six parameters are thus required to determine

TABLE II.

Observed Structure Factors.

hkl.	*F.*	*a.*	*hkl.*	*F.*	*a.*	*hkl.*	*F.*	*a.*	*hkl.*	*F.*	*a.*
000	148·0		501	5·4	217°	323	15·8	259°	325	8·1	180°
110	22·7	0°	521	9·3	325	343	12·1	82	345	<2·6	
130	<2·8		541	6·6	35	413	12·1	148	415	6·1	180
150	11·3	180	611	12·1	340	433	12·1	0	435	<2·4	
200	37·2	180	631	8·5	171	503	5·4	292	505	8·1	180
220	24·3	0	002	60·0	0	523	11·8	281	525	<2·5	
240	3·7	180	112	28·8	304	543	<2·4		006	10·4	0
260	4·9	0	132	11·4	342	613	12·1	323	116	4·7	101
310	12·3	180	152	10·5	159	004	16·2	0	136	13·5	3
330	12·6	0	202	32·4	190	114	20·9	262	206	6·1	165
350	9·7	0	222	32·2	323	134	24·1	357	226	11·4	25
400	5·3	0	242	6·0	106	154	<2·4		246	<2·6	
420	7·4	0	262	8·9	20	204	14·0	193	316	10·5	82
440	7·6	0	312	8·1	246	224	19·8	336	336	<2·6	
510	14·8	0	332	5·4	354	244	<2·4		406	15·1	326
530	3·2	0	352	10·1	47	314	6·6	278	426	<2·6	
600	5·8	0	402	11·1	17	334	2·6	183	516	9·8	66
620	<2·8		422	6·6	67	354	<2·4		107	5·4	164
101	22·1	354	442	<2·6		404	19·1	5	127	11·4	82
121	12·3	237	512	16·7	323	424	6·1	174	147	4·7	349
141	5·4	66	532	<2·4		444	<2·6		217	12·9	40
161	6·7	3	602	7·7	301	514	13·2	335	237	<2·6	
211	33·0	332	622	<2·6		534	<2·4		307	8·1	12
231	23·8	187	103	17·7	204	604	6·6	131	327	<2·6	
251	16·4	23	123	8·1	278	105	11·4	180	417	<2·4	
301	10·1	340	143	13·8	13	125	11·8	0	008	11·1	0
321	11·0	318	163	<2·6		145	16·2	0	118	<2·6	
341	10·4	34	213	36·2	321	215	16·4	0	138	4·7	32
411	18·7	167	233	12·3	191	235	5·4	180	208	5·4	166
431	29·8	0	253	16·6	30	255	7·2	0	228	7·6	36
451	8·5	171	303	26·3	347	305	21·4	0	318	5·4	50

the structure. The only symmetry is that of the four-fold alternating axis (which is also a two-fold rotation axis) and the derived two-fold screw axes, all of which are parallel to [001].

The four parameters x_1, y_1, x_2, and y_2 were determined by two separate methods : (*a*) a Patterson–Harker synthesis using the data of Table II, (*b*) a Fourier analysis of the F-values of Table I. As Harker (*J. Chem. Physics*, 1936, **4**, 381) has shown, the x and y co-ordinates of all the atoms in a structure having a two-fold axis of symmetry parallel to the z-axis may be found from the positions of the maxima of the Patterson function $P(xy0)$ where

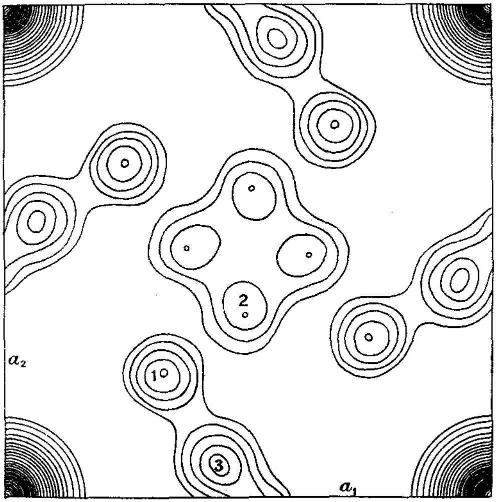
$$P(xy0) = \sum_h \sum_k \cos 2\pi(hx + ky) \, . \, (\sum_l |F(hkl)|^2)$$

Hence, corresponding to the separation of the two symmetrically related atoms at $(x\ y\ z)$ and $(\bar{x}\ \bar{y}\ z)$ in the crystal lattice, there will be a maximum in the value of $P(xy0)$ at $(2x, 2y)$. In addition there will be maxima in $P(xy0)$ corresponding to the separation of any two atoms which, although not related by the symmetry of the two-fold axis, have by chance the same, or nearly the same, z-co-ordinates.

The evaluation of $P(xy0)$ was carried out by the method of Beevers and Lipson (*Proc. Physical Soc.*, 1936, **48**, 772), the squares of all the F values listed in Table II being used. A diagram of the result is shown in Fig. 1, where the contours are plotted over a complete unit cell at intervals of 20 in the value of P, negative contours being omitted. On account of the tetragonal symmetry, every feature is repeated four times in the diagram, so there are actually three fundamental maxima, labelled 1, 2, and 3. (The large peak at the origin is merely an expression of the fact that every atom is at zero distance from itself.) Now in the case of pentaerythritol only two peaks can arise from the separation of atoms which are symmetrically related ("space-group maxima"), *viz.*, one with co-ordinates $(2x_1, 2y_1)$ corresponding to the separation of the carbon atoms in the general positions $(x_1y_1z_1)$ and $(\bar{x}_1\bar{y}_1z_1)$, and another with co-ordinates $(2x_2, 2y_2)$ similarly derived from symmetrically related oxygen atoms. The existence of a third peak shows that by chance two atoms other than those symmetrically related have nearly the same z-co-ordinates. Thus, either each CH_2 group and its attached hydroxyl group have the same z-co-ordinates (*i.e.*, $z_1 \simeq z_2$)

or the four CH_2 groups of each molecule are in the same plane with the central carbon atom (*i.e.*, $z_1 \approx 0$) or the four hydroxyl groups are coplanar with the central carbon atom (*i.e.*, $z_2 \approx 0$). Of these three possibilities it is easy to show on various grounds (by means of the intensities of the orders of {002}, etc.) that the last is actually correct. A further point which now arises is that if $z_2 \approx 0$, there should be, in addition to the two space-group maxima in Fig. 1, two other maxima, *viz.*, one with co-ordinates (x_2y_2) corresponding to the distance of the hydroxyl groups from the carbon at the origin, and another with co-ordinates $(x_2 + y_2, y_2 - x_2)$ corresponding to the distance apart of two hydroxyl groups at (x_2y_20) and $(\bar{y}_2x_20)$. This apparent discrepancy in the number of maxima is completely explained, and the peaks unequivocally assigned to their appropriate atomic

FIG. 1.



distances, when it is observed that the co-ordinates of peak 2 are nearly double those of peak 1. Thus the peak 2 is a space-group maximum representing the O–O separation and has co-ordinates $(2x_2, 2y_2)$, the peak 3 is one of the chance maxima with co-ordinates $(x_2 + y_2, y_2 - x_2)$ giving another O–O distance, and the peak 1 is formed by the superposition of two maxima, one the carbon–carbon space-group maximum $(2x_1, 2y_1)$ and the other a chance carbon–oxygen maximum (x_2y_2). Thus from the Patterson–Harker synthesis we find the following atomic co-ordinates (expressed as fractions of the length of the *a*-axis):

$$\text{Carbon, } x = 0{\cdot}161,\ y = 0{\cdot}123$$
$$\text{Oxygen, } x = 0{\cdot}314,\ y = 0{\cdot}247,\ z \approx 0$$

Owing to the overlapping of the two maxima in peak 1, the values of the carbon co-ordinates are not quite so accurate as those of the oxygen.

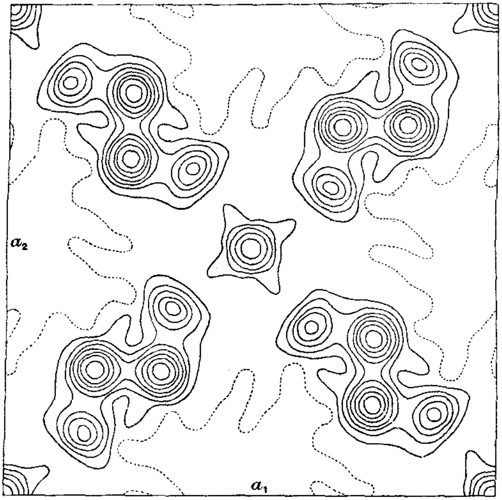
The *x* and *y* co-ordinates were next determined more accurately by means of a two-dimensional Fourier projection of the content of the unit cell on (001), using the *F*-values for all the [*hk*0] planes recorded in Table I. [A projection was originally made with the data obtained with copper radiation only, but it was found that the inclusion of the results

obtained with molybdenum radiation (all F-values from planes with d less than 0·90 A.) greatly improved the resolution.] The projection on (001) is centro-symmetrical, and the expression for the electron density takes the form

$$\rho(xy) = \sum_{-\infty}^{\infty} \sum_{-\infty}^{\infty} F_{hk0} \cos 2\pi(hx + ky)$$

so it was only necessary to determine whether the F's are positive or negative; this was done by calculating the structure factors of all the $\{hk0\}$ planes from the atomic co-ordinates obtained in the Patterson synthesis. Since for this purpose great accuracy is unnecessary,

FIG. 2.



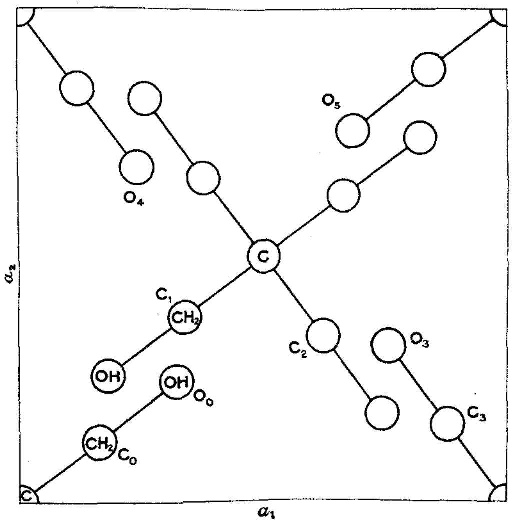
much of the calculation was eliminated by using structure contour graphs of the type proposed by Bragg (*Nature*, 1936, **138**, 362; see also Bragg and Lipson, *Z. Krist.*, 1936, **95**, 323). At later stages where calculation was considered necessary, and also in dealing with zones of lower symmetry where the advantage of structure factor graphs is not so marked, it was found helpful to construct a table of the function $y = A\cos 2\pi x$, computed for values of x from 0 to 1·00 at intervals of 0·01 and for values of A from 1·0 to 10·0 at intervals of 0·2. Such a table can be prepared in a few hours with the aid of a multiplying machine, and results in great saving of time when many structure factors have to be calculated.

The Fourier synthesis was carried out by the procedure of Beevers and Lipson (*loc. cit.*) with the result shown in Fig. 2, which gives a projection of one complete unit cell on (001), the contours being drawn at intervals of one electron per sq. A., with the one-electron contour dotted. All the atoms in the cell are clearly resolved, and their x and y co-ordinates can be determined with considerable accuracy. Fig. 3 shows how the various peaks in the contour diagram are to be assigned to their respective atoms, while the co-ordinates of the atoms in the general positions are as follows:

Carbon, $x = 0{\cdot}162$, $y = 0{\cdot}123$
Oxygen, $x = 0{\cdot}317$, $y = 0{\cdot}247$

These values appear to be somewhat more reliable than those from the Patterson synthesis, and they have been adopted as final, but it should be observed that the very close agreement between the two sets of figures affords strong evidence as to the accuracy of both, since they have been determined from substantially different data (in the one case from all the $\{hk0\}$ planes with d greater than 0·50 A., and in the other from all $\{hkl\}$ planes with d greater than 0·90 A.). The structure factors calculated from the final co-ordinates are recorded in Table I under $F_{\text{calc.}}$; the figures depend to some extent on the particular atomic scattering factors used in the calculations, but the general agreement with the experimental data is quite satisfactory.

FIG. 3.



The z-co-ordinates were also determined both by the Patterson synthesis and by the usual Fourier method. It has already been shown that the oxygen co-ordinate (z_2) is approximately zero, while from a one-dimensional Fourier synthesis of the orders of $\{002\}$ it was found that the carbon co-ordinate (z_1) is about 0·10. Consideration of these results showed that the atomic positions were such that in a Fourier projection on either (100) or (110) the resolution would be to poor to fix the z-co-ordinates with sufficient accuracy. In order to make the best use of the experimental data it was therefore decided to determine the z-co-ordinates by calculating three-dimensional syntheses along lines which were known from two-dimensional results to pass through the atomic centres. Thus the distance apart of the carbon atom at (000) and the carbon atom at $(x_1y_1z_1)$ will be represented by a maximum in the value of the Patterson function $P(xyz)$ at the point $(x_1y_1z_1)$, so that z_1 can be found by evaluating the function

$$P(xyz) = \sum_{-\infty}^{\infty}\sum_{-\infty}^{\infty}\sum_{-\infty}^{\infty} |F_{hkl}|^2 \cos 2\pi(hx + ky + lz)$$

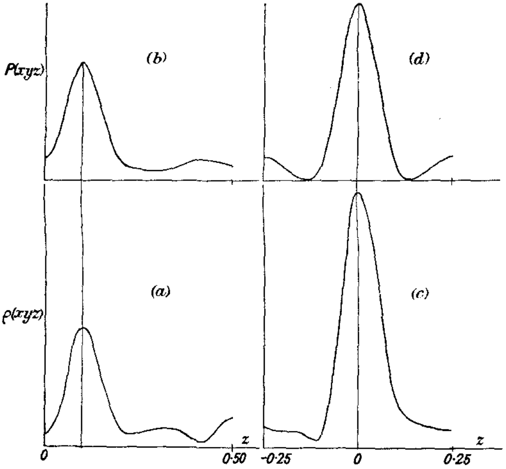
along the line (x_1y_1z) where x_1 and y_1 are the values already determined from the c-axis

projections, and finding the value of z_1 for which P is a maximum. In addition z_1 can be determined by finding the maximum electron density when the function

$$\rho(xyz) = \sum_{-\infty}^{\infty} \sum_{-\infty}^{\infty} \sum_{-\infty}^{\infty} F_{hkl} e^{2\pi i(hx+ky+lz)}$$

is plotted along the line (x_1y_1z), and both processes can be repeated to find z_2. It should be noted that the z-co-ordinates obtained by these methods are unaffected by small errors in the values of x and y co-ordinates used, since around the maxima in the three-dimensional Patterson and simple F syntheses the contour surfaces are nearly spherical and therefore the appropriate function plotted along a line which does not quite pass through the true centre will still show a maximum at the correct value of z.

FIG. 4.



(a) Electron density $\rho(xyz)$ along the line (0·162, 0·123, z).
(b) The function $P(xyz)$ along the line (0·162, 0·123, z).
(c) Electron density $\rho(xyz)$ along the line (0·317, 0·247, z).
(d) The function $P(xyz)$ along the line (0·317, 0·247, z).

The graphs of the functions $P(x_1y_1z)$ and $P(x_2y_2z)$ (based on all the F-values of Table II) are shown in Fig. 4 (b) and 4 (d) respectively, the maxima occurring at $z_1 = 0{\cdot}096$ and $z_2 = 0{\cdot}000$. While these results would normally be of high accuracy, they require slight adjustment in this particular case on account of the combined effects of a nearly zero value of z_2 and of symmetry parallel to (001) which is introduced as a consequence of the use of F^2 terms in the Patterson method. Thus, the peak in Fig. 4 (d) is actually due to superposition of two maxima at $\pm z_2$, while in Fig. 4 (b) the maxima at $(x_1y_1z_1)$ and $(x_2 - x_1, y_2 - y_1, z_1 - z_2)$ combine to give the observed result. On this account, although the values of z_1 and z_2 are probably very close to 0·096 and 0·000 respectively, yet the Fourier syntheses, in which use is made of the phase relations between the F's with the consequent elimination of spurious symmetry, will be more reliable. Since the crystals have no symmetry except in the c-zone, the evaluation of the Fourier syntheses involved a knowledge of the phase angles (α) of all the structure factors in Table II; these were calculated from the previously

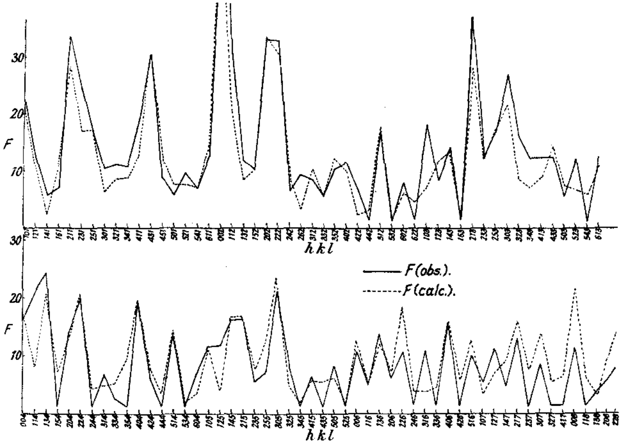
determined x and y co-ordinates and from the z-co-ordinates obtained from Figs. 4 (b) and 4 (d) and are given in Table II. The resultant graphs of electron density, which are not symmetrical about the origin, are shown in Figs. 4 (a) and 4 (c). The final values obtained from these graphs are $z_1 = 0{\cdot}097$ and $z_2 = 0{\cdot}002$.

The co-ordinates which, together with the operations of the space-group $I\bar{4}$, completely determine the structure are thus:

(000) for the carbon atom in the four-fold position, (0·162, 0·123, 0·097) for the carbon atom in the general position, and (0·317, 0·247, 0·002) for the oxygen atom in the general position.

Fig. 5 shows graphically the agreement between the experimental structure factors (continuous line) and those calculated from the above co-ordinates (broken line) for all planes not included in Table I.

FIG. 5.



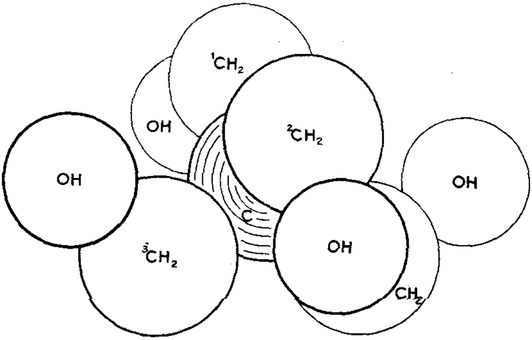
Discussion of the Structure.—A diagrammatic representation of the molecule of pentaerythritol as determined by the preceding analysis is shown in Fig. 6 (in which the vertical direction is parallel to the c-axis). The central carbon atom (shaded) is surrounded by four CH_2 groups at the corners of an almost exact tetrahedron, and each hydroxyl group is attached to its CH_2 by a bond which makes a nearly tetrahedral angle with the C–CH_2 link and is so directed that the four hydroxyl groups lie at the corners of a square. It is of interest to note that this conformation is the same as that possessed by pentaerythritol halogenohydrins in the vapour state (de Laszlo, *Compt. rend.*, 1934, **198**, 2235) and probably also in the solid state if it is assumed that their space-group is $P2$ and not $P2/m$ as suggested by Wagner and Dengel (*Z. physikal. Chem.*, 1932, *B*, **16**, 382; cf. *Ann. Reports*, 1933, **30**, 416). The bond lengths and angles calculated from the measured atomic co-ordinates and cell dimensions are as follows:

Distances.	*Angles.*
C–C = 1·50 A.	^{1}C–C–^{2}C = 111½°
C–O = 1·46 A.	^{1}C–C–^{3}C = 108½°
	C–C–O = 111½°

We estimate the probable error in the bond lengths to be not more than ± 0·03 A., while the angles are probably accurate to ± 1°. Thus the divergences of the angles from the

true tetrahedral value of 109½° are scarcely more than the experimental error, but the length of the carbon–carbon bond appears to be definitely slightly less than that found in diamond and usually assumed for aliphatic compounds (*viz.*, 1·54 A.), and it is considerably less than the value 1·58 A. found in dibenzyl (Robertson, *Proc. Roy. Soc.*, 1935, *A*, **150**, 348) and in ammonium oxalate monohydrate (Hendricks and Jefferson, *J. Chem. Physics*, **1936**, **4**, 102). These last two compounds, however, can hardly be regarded as closely similar to pentaerythritol. No quantitative results are available with which the figure for the C–O link can be strictly compared, since this distance is known to depend to an appreciable extent upon the chemical nature of the groups involved, but the value 1·46 A. is almost exactly equal to the calculated sum of the half bond lengths of carbon and oxygen (see, *e.g.*, Sidgwick, "The Covalent Link in Chemistry," p. 85). If the present measurement is typical of primary alcohols, it appears that the C–O distance in such compounds is the same as or slightly greater than in ethers or cyclic acetals, while it is definitely greater than in phenols, acids, etc. (for comparative figures, see *Ann. Reports*, 1936, **33**, 220).

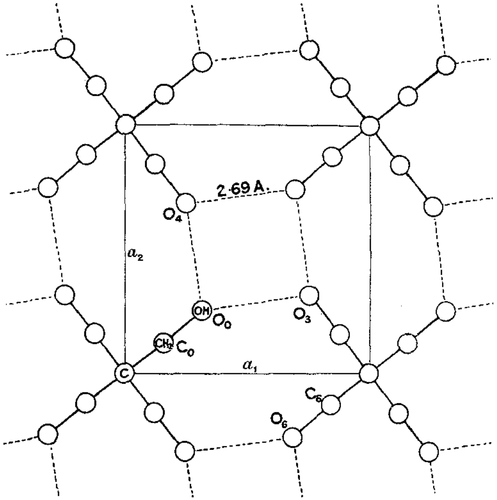
Fig. 6.



The structure of the lattice as a whole is of a very pronounced layer type; the molecules are linked together by hydroxyl bonds in sheets in the (002) planes, the separation of the sheets being more than 3½ A., thus accounting for the perfect cleavage parallel to {001}. The structure of one of the sheets is shown in Fig. 7, in which the distance of closest approach of hydroxyl groups is shown by broken lines. The minimum separation of oxygen atoms is 2·69 A., and although it is impossible to determine the position of the hydrogen atoms by *X*-rays methods, there is a very strong accumulation of evidence to support the view that this relatively short distance between hydroxyl groups represents a "hydroxyl bond" in which a hydrogen atom binds two oxygen atoms closely together while remaining attached essentially to one of them. Each hydroxyl group in pentaerythritol has two such bonds both nearly in the (002) plane, making an angle of nearly 90° with each other and inclined at 137° and 115° respectively to the carbon–oxygen bond, which is not coplanar with them. This arrangement is similar to that observed in various other instances where hydroxyl bonds have been suggested; in particular there is marked resemblance to the case of resorcinol (Robertson, *Proc. Roy. Soc.*, **1936**, *A*, **157**, 79) both in the oxygen–oxygen distance (mean value 2·70 A.) and in the environment of the oxygen atoms (apart from the shorter carbon–oxygen distance). In so far as resorcinol and pentaerythritol are typical of phenols and alcohols respectively, this resemblance is noteworthy in suggesting that the differences between the two classes of compound in the solid state do not extend to the extra-molecular relations of the oxygen atoms, in contrast with the appreciable divergence inside the molecule as expressed by the respective carbon–oxygen separations (1·36 and 1·46 A.). It is

reasonably safe to infer that the differences between primary and secondary alcohols in this respect are at least no greater than those between the former and the phenols, and the linking together of secondary alcohols (*e.g.*, sugars) in the solid state is effected by means of hydroxyl bonds whose lengths do not differ greatly from 2·70 A., two such bonds to each oxygen atom being probable.

FIG. 7.



All other inter-molecular distances are very much greater than 2·7 A., and correspond to relatively weak van der Waals forces only; a complete list (up to 4·1 A.) is given below, the various atoms referred to being indicated in Figs. 3 and 7.

$O_0 - O_3 = 2·69$ A.	$O_0 - C_1 = 3·63$ A.	$O_0 - C_6 = 3·99$ A.
$O_0 - O_4 = 2·69$ A.	$O_0 - O_6 = 3·76$ A.	$O_0 - C_2 = 4·01$ A.
$O_0 - C_3 = 3·56$ A.	$O_0 - O_5 = 3·80$ A.	$C_0 - C_2 = 4·10$ A.

EXPERIMENTAL.

The pentaerythritol used in the present investigation was obtained from the Eastman Kodak Company and melted at 250° (uncorr.). Crystals up to 5 mm. or more linear dimensions were readily obtained by slow recrystallisation from aqueous alcohol, but caution was necessary in selecting individuals for *X*-ray measurements on account of the tendency to twinning on {100}. All crystals used for intensity measurements were therefore subjected to a preliminary examination by means of Laue or oscillation photographs to ensure that they were free from twinning, as indicated by the difference in intensities of the planes (*hkl*) and (*khl*).

The absolute intensities of the orders of {002}, {200}, and {101} were measured by reflection from natural and ground faces of large crystals or by transmission through appropriately cut parallel-sided sections, the experiments being carried out with the (400) rock-salt reflection as the standard of reference as previously described (Cox, Wardlaw, and Webster, J., 1936, 780). As an example of the consistency of these measurements, the following values of the structure factor *F* of (004) derived from a series of experiments may be quoted: 16·3, 16·5, 16·9, 15·5, 15·8, 16·2, 16·6, 15·9 (mean 16·2). The intensities of these planes were used to put all the others on the absolute scale by means of measurements on oscillation photographs of small crystals completely

bathed in the X-ray beam. For this purpose crystals were selected which, by reason of the equal development of {101} and {001}, were roughly spherical in form, so that there were no appreciable errors due to variable absorption of the X-ray beam. The {$h0l$} and {$hk0$} intensities were measured on a Cambridge microphotometer, care being taken to make measurements only within the photographic density range (up to 1·2 approximately) over which the density is proportional to the X-ray intensity. In the visual estimation of each {hkl} intensity, comparisons were made only with previously measured planes of nearly the same intensity. Where planes not on the equatorial line of the photographs were measured, the appropriate corrections (Cox and Shaw, *Proc. Roy. Soc.*, **1929**, *A*, **127**, 71) were made.

SUMMARY.

By means of quantitative X-ray measurements the structure of the tetragonal crystals of pentaerythritol has been completely determined. The interatomic distances within the molecule are C–C = 1·50 A. and C–O = 1·46 A., and the deviations of the bond angles from the tetrahedral value of 109½° are negligible. Each hydroxyl group is linked to two others in neighbouring molecules by " hydroxyl bonds " of length 2·69 A., in such a way that a layer structure with pronounced basal cleavage results.

We are indebted to H.M. Department of Scientific and Industrial Research for a Senior Award to one of us (T. H. G.), and to Prof. W. N. Haworth, F.R.S., for his encouragement.

THE UNIVERSITY, BIRMINGHAM 15. [*Received, April 17th*, 1937.]

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184. *Usnic Acid. Part V.*

By FRANK H. CURD and ALEXANDER ROBERTSON.

THE experiments described in the present communication were carried out in 1932—33, and, although our studies on usnic acid are not yet completed, it is necessary, in view of the work of Asahina and Yanagita (*Ber.*, 1936, **69**, 1646), to place the results on record and to discuss their bearing on revised expressions possible for decarbousnic acid, decarbousnol, usnolic acid, and usnic acid. Until decisive evidence regarding the structures proposed in Part III (J., **1933**, **1173**) for pyrousnic acid and usnetic acid became available (Asahina and Yanagita, *loc. cit.*; Part IV, J., **1936**, 1834) this discussion on new formulations for these compounds did not appear profitable.

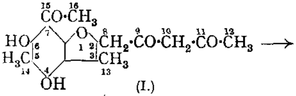
Decarbousnic Acid.

This compound is the main product of the reaction obtaining when usnic acid is heated with 96% alcohol under pressure (compare Paternò, *Gazzetta*, 1876, **6**, 113; Widman, *Annalen*, 1900, **310**, 230, 265; 1902, **324**, 139) and, although the reaction mechanism involved is still obscure, the process is regarded as being essentially one of hydration and simultaneous loss of carbon dioxide. Whilst structures of the hemi-quinonoid type proposed for usnic acid and its degradation products by Schöpf and Heuck (*Annalen*, 1927, **459**, 233) are fundamentally unsound (compare Part III, J., **1933**, **1173**), the suggestion of these authors that decarbousnic acid contains the groups CH_3·CO· and ⫶C·CO·CH·CO·C⫶ and is not a carboyxlic acid affords a basis for a satisfactory explanation of its behaviour. Thus decarbousnic acid cannot be esterified or decarboxylated and the oxime anhydride, anhydrobisphenylhydrazone, and anilide described by Widman (*loc. cit.*) may be considered to be respectively *iso*oxazole, pyrazole, and anil derivatives. The presence of a 1 : 3-diketonic group in this compound also receives support from the fact that the product formed by interaction with semicarbazide hydrochloride has now been found to have the composition of a pyrazole derivative and not that of a hydrazone as Widman (*loc. cit.*) suggested. In this respect the behaviour of decarbousnic acid is strictly analogous to that of benzoylacetophenone (Posner, *Ber.*, **1901**, **34**, **3973**).

With a view to obtaining confirmatory evidence of the presence of a 1 : 3-diketonic

group in decarbousnic acid we have investigated the hydrolysis of the compound with warm aqueous potassium hydroxide and by this procedure have obtained acetic acid, acetone, usnetic acid (II), pyrousnic acid (III), and a compound $C_{15}H_{16}O_5$, and we have also observed that the particular combination of these products which can be conveniently detected in the reaction mixture is to some extent dependent on the conditions employed. Since it apparently arises from decarbousnic acid by loss of an acetyl group, the substance $C_{15}H_{16}O_5$ has been designated *deacetyldecarbousnic acid*. It is of interest to note that with the exception of this compound and of usnetinic acid (Part III, *loc. cit.*) the products of the hydrolytic fission of decarbousnic acid are identical with those formed from usnic acid under comparable conditions and, although so far as we are aware—and our own observations confirm this—decarbousnic acid has never been obtained from usnic acid by hydrolytic fission with warm aqueous sodium or potassium hydroxide, the present results suggest that it may be an intermediate stage in this degradation.

The behaviour of decarbousnic acid on hydrolysis in conjunction with the nature of the products formed with ketonic reagents affords conclusive evidence that this compound is a 1 : 3-diketone which may be regarded as being derived from usnetic acid by the addition of acetone with the elimination of the elements of water and the suppression of the carboxyl group (*i.e.*, the reversal of one type of hydrolysis) and thus, in agreement with the suggestion of Asahina and Yanagita (*loc. cit.*), may be represented by the formula (I).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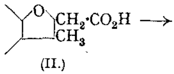
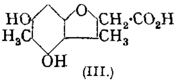

(II.)

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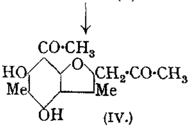
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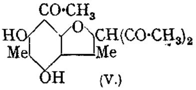
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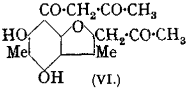
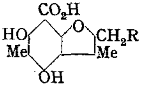
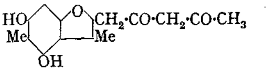

(VI.)

(VII.)


(VIII.)

The expression (I) can be justified experimentally in every detail and, apart from the formation of decarbousnol which will be discussed later, affords a satisfactory explanation of the main properties and reactions of decarbousnic acid.

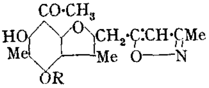
(1) Decarbousnic acid obtained from *d*- or *l*-usnic acid is always optically inactive and therefore presumably does not contain an asymmetric carbon atom, a conclusion which is supported by the fact that Schöpf and Heuck (*loc. cit.*) observed that *d*-diacetylusnic acid also gave rise directly to an inactive diacetyl derivative of decarbousnic acid.

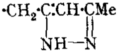
(2) The behaviour of the compound on titration as a dibasic acid is explained by the presence of an acidic enolic group * and of the phenolic hydroxyl group in the 4-position, the acidity of which is enhanced by the *C*-acetyl group in the 7-position.

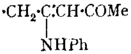
(3) Formula (I) affords a satisfactory explanation of the behaviour of decarbousnic acid with ketonic reagents. The *iso*oxazole and pyrazole derivatives obtained by oximation and by the action of semicarbazide hydrochloride (compare Posner, *loc. cit.*) may be

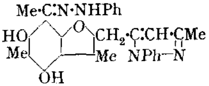
* Two structures are possible for the enolic form of a diketone of the type (I), *viz.*, (A) R·CH₂·C(OH):CH·CO·CH₃ and (B) R·CH₂·CO·CH:C(OH)·CH₃ [R·CH₂·CO·CH₂·C(OH):CH₂ is unlikely], and similarly there are two possible formulæ for the *iso*oxazole and pyrazole derivatives, depending on whether decarbousnic acid reacts as (A) or (B). Only one set of formulæ is employed in the present communication, although it is recognised that the respective alternative structures are equally possible.

represented by formula type (IX, R = H) and (X, R = H) respectively, whilst the anilide of Widman is the anil type (XI, R = H).

(IX.) 

 (X.)

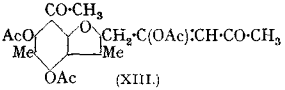
(XI.) 

 (XII.)

By heating the *iso*oxazole (oxime anhydride) with acetic anhydride, Widman (1900) obtained a monoacetyl derivative which was insoluble in aqueous sodium hydroxide but gave a green ferric reaction. Since it is well known that in a compound of the type (IX, R = H) the hydroxyl group at the 4-position is preferentially acylated or methylated, Widman's acetate must have formula type (IX, R = Ac), a view which is in agreement with the fact that the behaviour of the acetate towards sodium hydroxide and alcoholic ferric chloride is similar to that of usnetol monomethyl ether and of methyl 4-*O*-methylusnetate (Part III, *loc. cit.*).

In the condensation of decarbousnic acid with phenylhydrazine both the 1 : 3-diketonic and the 7-acetyl groups react, giving rise to an anhydrobisphenylhydrazone which must have the pyrazole structure type (XII).

(4) Mono-, di-, tri-, and tetra-acetyl derivatives of decarbousnic acid (Widman, *loc. cit.*; Schöpf and Heuck, *loc. cit.*) have been described and, although it is not possible at present to allocate definite formulæ to the mono- and the di-acetyl derivative, the triacetyl compound, which has a negative ferric reaction, has presumably the structure type (XIII), whereas the golden-yellow tetra-acetyl derivative may be of the type (XIV) or (XV).



(XIII.)

$\cdot CH{:}C(OAc)\cdot CH{:}C(OAc)\cdot CH_3$

(XIV.)

$\cdot CH{:}C(OAc)\cdot CH(CO\cdot CH_3)_2$

(XV.)

(5) The structure (I) for decarbousnic acid provides a rational explanation of the formation of the products of hydrolysis, including deacetyldecarbousnic acid. Although the latter compound, which sublimes unchanged in a high vacuum, behaves on titration as a monobasic acid, it does not contain a carboxyl group and does not dissolve in aqueous sodium bicarbonate or react with warm aniline. On the basis of the expression (I) for decarbousnic acid the deacetyl derivative may be represented by formula (IV), whereby its behaviour as a monobasic acid on titration is accounted for by the enhanced acidity of the phenolic hydroxyl group at the 4-position due to the presence of the *C*-acetyl group at the 7-position. This formulation is in agreement with the fact that the compound gives the same characteristic ferric reaction as usnetic acid and usnetol (Part III, *loc. cit.*) and forms a diacetate which is insoluble in aqueous sodium hydroxide and has a negative ferric reaction. The alternative structure (VIII) for deacetyldecarbousnic acid is excluded because a compound of this type would be expected to give the red or red-brown ferric reaction characteristic of the group $\cdot CO\cdot CH_2\cdot CO\cdot$ (the pyrousnyl residue does not give a coloration with alcoholic ferric chloride; Part III, *loc. cit.*) and to form an *O*-diacetyl derivative soluble in aqueous sodium hydroxide.

In the conversion of usnic acid into decarbousnic acid Widman (*loc. cit.*) obtained a by-product, m. p. 197°, which he considered to be an isomeride of the latter and named *iso*decarbousnic acid. This substance, which in one experiment was the main product of the reaction, has been found to be deacetyldecarbousnic acid (IV).

The alternative possible formulæ, (V) and (VI), for decarbousnic acid which also embody

a 1 : 3-diketonic group can be excluded from a consideration of the behaviour of the compound on hydrolytic fission. Although both the expressions (V) and (VI) can account for the formation of deacetyldecarbousnic acid (IV), neither is compatible with the formation of usnetic acid (II) and of pyrousnic acid (III); *e.g.*, the products of the alkaline hydrolysis of (VI) would not be usnetic acid and pyrousnic acid but their respective isomerides (VII, R = Ac) and (VII, R = H), whereas compounds of this type have never been encountered among the degradation products of decarbousnic acid or of usnic acid.

Usnic Acid.

The formulation of this compound may be expressed as a reversal of the process obtaining in the formation of decarbousnic acid, *i.e.*, by the addition of a carboxyl group with the elimination of the elements of water. Apart from the formation of usnolic acid (compare decarbousnol) the main criteria which must be satisfied by any formula for usnic acid may be grouped as follows :—

(1) Usnic acid contains an asymmetric carbon atom which appears to be destroyed in the conversion of usnic acid into the isomeride usnolic acid and into decarbousnic acid.

(2) The view expressed by Schöpf and Heuck that the acidic properties of usnic acid are due to the presence of a highly acidic enolic group as in decarbousnic acid is an essential feature. Although it does not appear to contain a carboxyl group, usnic acid titrates as a monobasic acid, a phenomenon which can hardly be explained by the opening of a lactone ring because we have found that acidification of a solution of the *l*-isomeride in dilute aqueous sodium hydroxide, which has been kept for a short time, gave unchanged material, having the initial rotatory value. This view is also strongly supported by the fact that Schöpf and Heuck (*loc. cit.*) found that deacetylation of *d*-diacetylusnic acid with hot dilute aqueous sodium hydroxide yielded *d*-usnic acid.

(3) According to the Zerewitinoff method usnic acid contains three active hydrogen atoms (Schöpf and Heuck, *loc. cit.*), and, although in a compound of this type conclusions drawn from Zerewitinoff determinations cannot be relied on entirely, this result is supported by the fact that the diacetyl derivative behaves on titration as a monobasic acid and gives a wine-red ferric reaction. Although a phenolic hydroxyl group in the *o*-position to a carbonyl group would account for the coloration with alcoholic ferric chloride, this group would exhibit an abnormally low acidity due to chelation and therefore these results suggest that diacetylusnic acid and consequently usnic acid contain an acidic enolic group, thus rendering unnecessary the assumption that the behaviour of these compounds on titration is due to the opening of a lactone ring system.

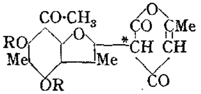
(4) In addition to forming a normal oxime, a semicarbazone, and a phenylbenzylhydrazone, usnic acid yields an oxime anhydride and an anhydrobisphenylhydrazone (Widman, *loc. cit.*; Schöpf and Heuck, *loc. cit.*), whereby it closely resembles decarbousnic acid. On the view that usnic acid contains a lactone group the last two derivatives might well be an *iso*oxazolone and a pyrazolone, respectively derived from a potential β-ketonic acid, but the production of compounds of this type implies a complex change involving the opening of the lactone ring system with subsequent dehydration of the resulting *iso*oxazolone and pyrazolone. It would appear to be more likely that, as in the case of the corresponding decarbousnic acid derivatives, the oxime anhydride and anhydrobisphenylhydrazone of usnic acid are respectively *iso*oxazole and pyrazole derivatives, implying the presence of a 1 : 3-diketonic system in the molecule (compare Asahina and Yanagita, *loc. cit.*). Further, both carbonyl groups of this residue cannot be present in a ring system, because compounds like the alkyl- and phenyl-dihydroresorcinols have been shown by Vorländer (*Annalen*, **1897**, **294**, 253) to form normal mono- and di-oximes and do not give *iso*oxazoles, and the phenylhydrazone of ethyl dihydroresorcylate cannot be converted into a pyrazole derivative (Knoevenagel, *Ber.*, 1894, **27**, 2343).

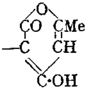
The presence of a β-ketonic group in usnic acid also accounts for the formation of an anil (the anilide of Widman, *loc. cit.*). Since this derivative has been obtained in *d*-, *l*-, and racemic forms and the anhydrobisphenylhydrazone in the *d*- and racemic forms, the enolisation of the diketonic group on which their formation depends does not involve the asymmetric carbon atom.

(5) With the exception of deacetyldecarbousnic acid and usnetinic acid the products of the hydrolytic fission of usnic acid with alkali are identical with those obtained from decarbousnic acid.

(6) *Although a lactone group has been considered to be an essential feature of the* usnic acid molecule (Widman; Schöpf and Heuck; Asahina and Yanagita, *locc. cit.*), it must be emphasised that, apart from the conversion of usnic acid into the isomeride usnolic acid, the mechanism of which is still obscure, there is no satisfactory evidence indicating the presence of this group and it may well be that the >CO group, which is eliminated in the conversion of usnic acid into decarbousnic acid and which appears as the carboxyl group of usnolic acid (see section on Usnolic Acid), is originally present as a ketonic and not as a lactone group. The experiments on the deacetylation of diacetylusnic acid by Schöpf and Heuck (*loc. cit.*) and our own observations on the action of cold aqueous sodium hydroxide on usnic acid indicate that the lactone group if present is either stable to alkali under those conditions or is instantaneously re-formed on liberation of the parent acid from the sodium salt.

On the view that usnic acid is a lactone derived from decarbousnic acid it would seem likely, since decarbousnic acid does not contain an asymmetric centre and on this view would in all probability be formed by the hydration of the lactone group and subsequent loss of carbon dioxide, that, in the system $\vdots C_\alpha \cdot C_\beta O \cdot O \cdot C_\gamma \vdots$, C_α is the asymmetric centre and not C_γ. Accordingly, structures which do not have this type of formulation need not be considered; thus formulæ which have the lactone group attached at the 12-, 13-, 14-, or *16-position of decarbousnic acid (I) are excluded. Of the remaining possibilities, viz.*, the attachment of the lactone group at the 8- or 10-position of (I), the latter implies a β-lactone structure and the former leads to the formulation of usnic acid as a pyronone (XVI, R = H) where the carbon atom at the 3-position (marked *) is asymmetric, a structure which has been proposed by Asahina and Yanagita (*loc. cit.*).

(XVI.) 

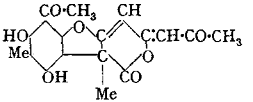
 (XVII.)

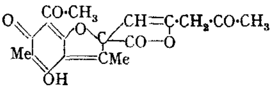
Although the expression (XVI, R = H) for usnic acid accounts for the products formed by alkaline hydrolysis and the formation of decarbousnic acid, it fails to explain the behaviour of the compound as a 1 : 3-diketone in forming an oxime anhydride and an anhydrobisphenylhydrazone without assuming a complex change which is difficult to formulate. Further, a compound having a pyronone type of structure (XVI, R = H) would be expected to exist in the enolic form (XVII, R = H) (*e.g.*, compare 4-hydroxy coumarins) and in any case, if the compound were normally obtained in the ketonic form, enolisation with consequent loss of optical activity would take place in the presence of aqueous sodium hydroxide. Moreover, the properties, *viz.*, titration as a monobasic acid and red ferric reaction, of the diacetate, which on this formulation would presumably be (XVI, R = Ac), indicate the presence of an enolic group. On these grounds, therefore, the expression (XVI, R = H) for usnic acid is regarded as untenable.

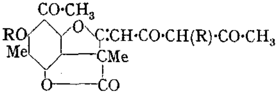
In attempting to deduce a new formulation for usnic acid embodying the essential properties enumerated in sections 1—6 inclusive (pp. 897—898), we have considered the question as to whether the molecule contains the benzofuran residue of usnetic acid and, though the evidence at our disposal clearly indicates that the benzofuran skeleton is intact in usnic acid, this system may exist in a modified form as in formulæ (XVIII), (XIX), and (XX, R = H).

Of these, the expression (XX, R = H), which retains the 1 : 3-diketonic system of decarbousnic acid, accounts for the following properties of usnic acid: optical activity, titration as a monobasic acid due to an acidic enolic group, behaviour with ketonic reagents, formation of the products of hydrolysis, and the conversion into decarbousnic acid by opening of the lactone ring and the extrusion of the carboxyl group due to the tendency of the system to revert to the more stable benzofuran type (I). In formulating the acidic diacetyl derivative on the basis of the structure (XX, R = H) it is necessary to assume that

one of the acetyl groups is attached to a carbon atom of the 1 : 3-diketonic system as in (XX, R = Ac), an expression which would also account for the acidic properties and the

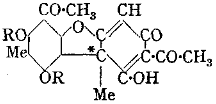

(XVIII.)

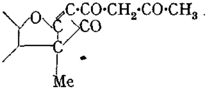

(XIX.)

(XX.)


ferric reaction due to the presence of an enolic group. It is less easy, however, to explain the deacetylation of this diacetyl compound by warm dilute aqueous sodium hydroxide with the recovery of unchanged usnic acid (Schöpf and Heuck, *loc. cit.*), because it is unlikely on stereochemical grounds that the lactone ring system in (XX) has a stability comparable with that of an α-coumaranone.

Although on the evidence which is available at present formula (XX, R = H) is clearly a more satisfactory expression for usnic acid than (XVI, R = H) it seems desirable, in view of the aforementioned deficiencies of (XX, R = H), to consider the alternative possibility, *viz.*, that usnic acid does not contain a lactone group. This implies that the >CO group of usnic acid, which is lost on conversion of the compound into decarbousnic acid, is originally present as a ketonic and not as a lactone group. On this view we may formulate usnic acid as (XXI, R = H) or (XXII, R = H), of which only the former need be considered at present. This structure, where ring C is a *gem*-substituted phloroglucinol residue similar to that present in filicinic acid and its derivatives (J., 1933, 1617), would account for the optical activity of usnic acid, the products obtained on hydrolysis, the behaviour with ketonic reagents and with aniline, the presence of three active hydrogen atoms as indicated by the Zerewitinoff method, and the properties of the diacetate, which presumably would be (XXI, R = Ac).

(XXI.)



(XXII.)

Whilst by analogy with decarbousnic acid a compound of the type (XXI, R = H) might be expected to titrate as a di- and not as a mono-basic acid, a more serious objection to the structure (XXI, R = H) is the difficulty of explaining the conversion of usnic acid and its diacetate, respectively, into decarbousnic acid and diacetyldecarbousnic acid (Schöpf and Heuck, *loc. cit.*). To account for this reaction it is necessary to assume, as is not unreasonable, that the asymmetric carbon atom (marked *) accommodating the angular methyl group is a centre of weakness.

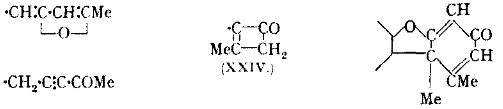
The available experimental evidence does not allow us to make a clear decision between the two types of structure (XX, R = H) and (XXI, R = H) which appear possible for usnic acid but it is of interest to note that the latter formula is derived by the union of two identical *C*-methylphloracetophenone units and is related to the diphenyl ether residue of the depsidone type of lichen acid.

Decarbousnol and Usnolic Acid.

The formation of decarbousnol by dehydration of decarbousnic acid with concentrated sulphuric acid and the isomerisation of usnic acid to usnolic acid by the same reagent have been confirmed (compare Paternò, *Gazzetta*, 1900, 30, 109; Widman, *loc. cit.*). Though the expression (I) for decarbousnic acid does not offer a clear explanation of the former re-

action, for which we have been unable to find an analogy in the literature, there appear to be four possible ways in which the dehydration product of a 1 : 3-diketone of this type may be expressed, *viz.*, (XXIII), (XXIV), (XXV) and (XXVI), of which (XXV) is regarded as highly improbable.

(XXIII.) (XXIV.) (XXV.) (XXVI.)



The remaining structures account for the following properties of decarbousnol: behaviour as monobasic acid on titration, inability to form an anil owing to the suppression of the 1 : 3-diketonic group, the green ferric reaction, and the formation of a monoacetyl derivative which is almost insoluble in aqueous sodium hydroxide but gives a blue-green ferric reaction.

Usnolic acid, which behaves on titration as a dibasic acid, contains one carboxyl group and forms monomethyl and monoethyl esters, both of which yield normal mono-oximes (compare Widman, *loc. cit.*). On decarboxylation this acid has now been found to yield decarbousnol, thereby clarifying the relationship of the two compounds. This result, together with the conversion of usnolic acid into the anil of decarbousnic acid by means of warm alcoholic aniline (Widman, *loc. cit.*), which we have confirmed, affords clear proof that the carbon atom which is lost in the degradation of usnic acid to decarbousnic acid appears as the carboxyl group of usnolic acid. Further, the interaction of the potential 1 : 3-diketonic group of usnolic acid with aniline is clearly dependent on the presence of the carboxyl group, because decarbousnol cannot be induced to react with aniline under similar conditions (compare Widman, *loc. cit.*). In connexion with this reaction it is of interest to note that the anil of phenyldihydroresorcylic acid is readily decarboxylated (Vorländer, *Annalen*, 1897, **294**, 253) under conditions similar to those employed in the conversion of usnolic acid into the decarbousnic acid anil.

Experimental.

Deacetyldecarbousnic Acid.—This compound was isolated in the course of the preparation of decarbousnic acid according to Widman's procedure (*Annalen*, 1900, **310**, 265). A mixture of usnic acid (5 g.), 96% alcohol (20 c.c.), and ether (1 c.c.) was heated in a sealed tube at 150—160° for 6 hours, more alcohol was added to the reaction mixture, and the resulting solution was evaporated in a vacuum at room temperature. The crystalline material which separated first consisted of almost pure decarbousnic acid (2·8 g.) and on recrystallisation from alcohol formed clusters of pale yellow needles, m. p. 178—179° (Found: C, 64·3; H, 5·9. Calc. for $C_{17}H_{18}O_6$: C, 64·2; H, 5·7%). On being heated, the brilliant yellow solution of this compound in sulphuric acid becomes red, then brown, and finally purple-brown.

Semicarbazide hydrochloride (0·3 g.), dissolved in a little water, was added to a hot alcoholic solution of decarbousnic acid (0·5 g.), and the mixture heated on the water-bath for ½ hour. On isolation the *pyrazole* derivative separated from benzene, containing a little alcohol, in clusters of colourless needles, m. p. 237—238° [Found: C, 65·3; H, 6·1; N, 9·0. $C_{17}H_{18}O_4N_2$ (pyrazole) requires C, 65·0; H, 5·7; N, 8·9%. Calc. for $C_{17}H_{20}O_5N_2$ (hydrazone): C, 61·4; H, 6·0; N, 8·4%. Calc. for $C_{18}H_{19}O_5N_3$ (semicarbazone): C, 60·5; H, 5·3; N, 11·8%] (Widman, *Annalen*, 1900, **310**, 275, gave m. p. 237° for a compound obtained in a similar manner which he considered to be a hydrazone).

Evaporation of the liquors left after the separation of decarbousnic acid gave crystals of *deacetyldecarbousnic acid* (0·3 g.); a further quantity (0·25 g.) was obtained by concentration of the mother-liquor from the first crystallisation of crude decarbousnic acid. Purified from alcohol, this compound formed colourless, feathery laminæ, m. p. 199—200°, which gave a greenish-purple to purple-blue coloration with alcoholic ferric chloride (Found: C, 65·3; H, 5·8. $C_{15}H_{16}O_5$ requires C, 65·2; H, 5·8%). On titration with 0·1*N*-sodium hydroxide it behaves as a monobasic acid, forming a yellow solution (0·1099 g. required 4·0 c.c. of 0·1*N*-sodium hydroxide, giving *M*, 275. $C_{15}H_{16}O_5$ requires *M*, 276). The colorations given by deacetyldecarbousnic acid with hot sulphuric acid are very similar to those obtained with decarbousnic acid

except that on addition of water the final purple-brown colour is not discharged. On being treated with sulphuric acid under conditions whereby the latter substance is converted into decarbousnol (see below), deacetyldecarbousnic was recovered unchanged.

In one experiment on the preparation of decarbousnic acid the contents of the tube were not a thick jelly as described in the literature but consisted of masses of hard crystals which on isolation proved to be deacetyldecarbousnic acid, m. p. and mixed m. p. 199—200° after recrystallisation (Found: C, 65·3; H, 5·8%). A further small quantity of the same product was obtained from the alcoholic liquors, but decarbousnic acid could not be detected.

Treatment of the deacetyldecarbousnic acid (0·5 g.) with acetic anhydride (1 c.c.) and pyridine (3 c.c.) at 37° for 24 hours gave the *diacetate*, which separated from ethyl acetate–light petroleum and then dilute methyl alcohol in clusters of needles, insoluble in aqueous sodium hydroxide and having a negative ferric reaction; m. p. 146—147° (Found: C, 62·9; H, 5·8. $C_{19}H_{20}O_7$ requires C, 63·3; H, 5·6%).

Hydrolytic Fission of Decarbousnic Acid.—The following are typical of the results obtained: (A) The compound (2 g.) was heated with a solution of potassium hydroxide (4 g.) in water (10 c.c.) at 170—180° in an atmosphere of hydrogen for 10 minutes, and the cooled reaction mixture acidified with dilute sulphuric acid. Crystallisation of the precipitate from alcohol gave deacetyldecarbousnic acid in characteristic feathery laminæ, m. p. 198—199°, identified by comparison with an authentic specimen.

Pyrousnic acid was isolated with absolute ether from the aqueous filtrate left on separation of deacetyldecarbousnic acid and purified by crystallisation from ethyl acetate–light petroleum, forming colourless needles, m. p. 200—201°, identical with an authentic specimen (Found: C, 60·9; H, 5·3. Calc. for $C_{12}H_{12}O_5$: C, 61·0; H, 5·1%).

Distillation of the aqueous liquors left on removal of the pyrousnic acid with the frequent addition of water so as to keep the volume constant gave an acidic aqueous distillate, which was neutralised with *N*-potassium hydroxide and evaporated. On the addition of acetone, a filtered alcoholic solution of the residue deposited characteristic crystals of potassium acetate, which was converted into silver salt (Found: Ag, 64·4. Calc. for $C_2H_3O_2Ag$: Ag, 64·7%).

(B) A solution of decarbousnic acid (2 g.) was heated with 60% aqueous potassium hydroxide (15 g.) at 90—100° in an atmosphere of hydrogen for ½ hour. On treatment with 2 : 4-dinitrophenylhydrazine hydrochloride in hydrochloric acid the small amount of aqueous distillate gave a precipitate of acetone-2 : 4-dinitrophenylhydrazone, which on purification had m. p. 128° and was identical with an authentic specimen.

The cooled reaction mixture was acidified with dilute sulphuric acid, and the precipitate of usnetic acid purified by means of aqueous sodium bicarbonate and then by crystallisation from dilute acetic acid, forming clusters of pale yellow needles, m. p. 210° (decomp.) after sintering at 188—191°, identical in every way with an authentic specimen, m. p. 211° (decomp.) with slight sintering at about 190°.

Usnolic Acid.—This compound was prepared from usnic acid (2·5 g.) according to the method of Widman (*Annalen*, 1902, **324**, 174) and after being separated from a little unchanged usnic acid was purified by crystallisation from alcohol, forming greenish-yellow laminæ (0·5 g.), m. p. 213—215° (decomp.) (compare Stenhouse and Grove, J., 1881, **39**, 234; Zopf, *Annalen*, 1900, **313**, 327; Widman, *loc. cit.*). When an intimate mixture of this acid (0·25 g.) and Kahlbaum's " Naturkupfer " (1 g.) was heated in a high vacuum at about 210—220°, decarbousnol sublimed; on recrystallisation from benzene it formed greenish-yellow laminæ, m. p. 204—205°. After sublimation in a high vacuum this material had m. p. 206° and was identified by comparison with a specimen of decarbousnol, m. p. 208°, prepared by Widman's method (*Annalen*, 1902, **324**, 184) (Found: C, 68·2; H, 5·5. Calc. for $C_{17}H_{16}O_5$: C, 68·0; H, 5·3%). The two compounds had the same crystalline form, solubilities, and ferric reaction (green, in alcohol) and on being mixed melted at 206—207°. Decarbousnol forms a yellow solution in sulphuric acid which on warming becomes red, brown-red and finally brownish-purple.

When a mixture of usnolic acid (0·4 g.) and aniline (1·5 c.c.) was heated on the water-bath for 1 minute, carbon dioxide was evolved and a crystalline product separated; this was collected, washed with a little warm alcohol, and recrystallised from acetic acid, forming slender needles, m. p. 231—232°, identical in every way with a specimen of the anil prepared from decarbousnic acid, m. p. 231—232° (Found: N, 3·4. Calc. for $C_{23}H_{21}O_5N$: N, 3·6%) (compare Widman, *Annalen*, 1902, **324**, 183, who gives m. p. 235—236°).

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University of Liverpool. [*Received, April 9th*, 1937.]

185. *The Transference of Water. Part III. Its Dependence on Concentration in the Electrolysis of Barium Chloride Solutions.*

By Millicent Taylor and Violet R. Willcox.

In previous investigations on water transport (Part I, J., 1929, 2095; Part II, J., 1932, 2497) it was shown that, during the electrolysis of sodium chloride solutions, water moves from the anode to the cathode, and the quantity of water transported per faraday of electricity decreases with increase in temperature and with increase in concentration; it was concluded that the ions transport water with which they are not chemically combined. Experiments of a similar nature, urea again being used as inert reference substance, have now been carried out with barium chloride solutions. This substance was chosen as a typical salt of a bivalent metal on account of the comparative ease of purification and also because other important and accurate numerical data, such as the transport numbers of the ions and the conductivity of the salt in aqueous solution at various concentrations, were already available (Jones and Dole, *J. Amer. Chem. Soc.*, 1929, **51**, 1073; 1930, **52**, 2245).

The measurements were carried out at 25° with $0{\cdot}5M$- and $0{\cdot}25M$-solutions of barium chloride. The water transport was found to be very small, as compared with that occurring in corresponding solutions of sodium chloride under the same conditions. In both concentrations water appears to be transported to the cathode, and the quantity transported changes little with concentration although the transport number of the barium ion increases rapidly with increasing dilution.

Experimental.

The migration apparatus was identical with that used in the previous investigations (*locc. cit.*). The container for the stock solution was a large flask with the specially constructed stopper described by MacInnes and Dole (*J. Amer. Chem. Soc.*, 1929, **51**, 1124). Before the migration apparatus was filled, a stream of purified nitrogen, already saturated with water vapour by contact with a portion of the solution, was passed through the main solution and the migration apparatus. On rotation of the stopper of the container through 180°, the solution was driven over into the migration apparatus without further exposure to air.

The anode consisted of a tightly rolled cylinder of pure silver gauze (mesh 60 to the inch) covered, according to the directions of Jones and Dole (*loc. cit.*), with a spongy coating of metallic silver. As in all previous experiments, precipitated silver chloride of known weight was used for the cathode. The use of a silver spiral coated electrolytically with chlorine was found to result in slight alkalinity at the cathode, notwithstanding that air had been removed from the solution.

Materials.—The urea was purified as previously described (*loc. cit.*). Kahlbaum's purest barium chloride dihydrate (" for analysis with guarantee ") was invariably used; its purity was confirmed by the agreement between the results of the analysis of the solution and its composition as prepared.

Analytical Method.—In each experiment the solution was analysed before electrolysis by the method subsequently used for the analysis of each separate portion after electrolysis. The urea was estimated as already described, and the chlorine by the method of Richards and Wells, a platinum sponge Munroe crucible being used, together with a nephelometer to determine dissolved silver chloride. The order of accuracy was equal to that obtained with sodium chloride solutions (Part II, *loc. cit.*).

The electrometric method of MacInnes and Dole (*J. Amer. Chem. Soc.*, 1929, **51**, 1119) was discarded, for, with the limited amount of material available the possibility of undetected error in this method appeared to be greater than in the gravimetric method.

Results.—Four experiments were carried out within 0·1° of 25°, two with $0{\cdot}25M$- and two with $0{\cdot}5M$-barium chloride solutions, the urea being approximately $0{\cdot}1M$ in each case.

In each experiment, except No. 1, the results depend upon the analysis of five solutions in all, the anode, the cathode, and three separate middle portions. In Expt. 1 no data are recorded for the cathode solution. This is due to the fact that the cathode portion became alkaline during electrolysis, probably on account of the texture of the silver chloride electrode, which had been prepared by chlorinating a silver spiral. In all subsequent experiments, we reverted to the precipitated silver chloride electrode of the type found satisfactory in Part I (*loc. cit.*) in place of the chlorinated spiral. An exactly known weight of silver chloride was used in the electrode.

The analyses carried out followed exactly the scheme indicated by the detailed results recorded

in Part II for similar experiments with sodium chloride solutions. The duration of each experiment varied from 16 hours at 0·06 amp. for the more dilute solutions to 11 hours at 0·096 amp. for the more concentrated solutions. The results are summarised in Table I, n_w representing the total number of g.-mols. of water, n_s the number of g.-equivs. of barium chloride transported, $T_{\frac{1}{2}Ba}$ and T_{Cl} the true transport numbers, and $T^H_{\frac{1}{2}Ba}$ and T^H_{Cl} the Hittorf transport numbers of the ions. The ratio n_w/n_s gives the number of g.-mols. of water transported per equivalent of barium chloride, and n^F_w the number of g.-mols. of water transported per faraday. The number of equivalents of silver deposited in the coulombmeters during each experiment is also recorded.

Table I.

(i) *Approx.* 0·25M-$BaCl_2$ *solution.*

Temperature 25° ± 0·01°.

	Expt. 1.	Expt. 2.			
Compn. of soln., g.-mols./1000 g. $BaCl_2$	0·24056		0·25382		
Compn. of soln., g.-mols./1000 g. Urea	0·098325		0·098173		
	Anode.	Anode.	Cathode.	Mean.	Mean of Expts. 1 & 2.
n_w	0·00327	0·00633	0·00433	0·0053	—
n_s	0·01387	0·01396	0·01462	0·0143	—
Ag, equivs.	0·034674	0·034759	0·034753	0·034756	—
$T_{\frac{1}{2}Ba}$	0·40006	0·40155	0·42067	$0{\cdot}4111_1$	0·4056
T_{Cl}	0·59994	0·59845	0·57933	$0{\cdot}5888_9$	0·5944
$T^H_{\frac{1}{2}Ba}$	0·39920	0·39978	0·41945	$0{\cdot}4096_1$	0·4044
T^H_{Cl}	0·60080	0·60022	0·58055	$0{\cdot}5903_9$	0·5956
n_w/n_s	0·2361	0·4534	0·2962	0·375	0·305
n^F_w	0·094	0·182	0·125	0·153	0·124

Specific gravity of solution 1 = 1·0440 g./c.c.

(ii) *Approx.* 0·5M-$BaCl_2$ *solution.*

Temperature 25° ± 0·02°.

	Expt. 3.			Expt. 4.			
Compn. of soln., g.-mols./1000 g. $BaCl_2$		0·48058			0·47444		
Compn. of soln., g.-mols./1000 g. Urea		0·096786			0·10103		
	Anode.	Cathode.	Mean.	Anode.	Cathode.	Mean.	Mean of Expts. 3 & 4.
n_w	0·00910	0·0019	0·00555	0·01040	0·00639	0·00839	—
n_s	0·01489	0·01485	0·01487	0·01696	0·01691	0·01694	—
Ag, equivs.	0·038562	0·038511	0·038537	0·043967	0·043983	0·043975	—
$T_{\frac{1}{2}Ba}$	$0{\cdot}3864_3$	0·3854	0·3859	$0{\cdot}3856_3$	$0{\cdot}3842_4$	0·3850	0·3855
T_{Cl}	$0{\cdot}6135_7$	0·6145	0·6141	$0{\cdot}6143_7$	$0{\cdot}6157_6$	0·6150	0·6145
$T^H_{\frac{1}{2}Ba}$	$0{\cdot}3817_0$	0·3845	0·3831	$0{\cdot}3810_7$	$0{\cdot}3814_6$	0·3813	0·3822
T^H_{Cl}	$0{\cdot}6183_0$	0·6155	0·6169	$0{\cdot}6189_3$	$0{\cdot}6185_4$	0·6187	0·6178
n_w/n_s	0·611	0·127	0·369	0·612	0·378	0·499	0·434
n^F_w	0·231	0·0490	0·140	0·236	0·145	0·191	0·166

Specific gravity of solution 4 = 1·09235 g./c.c.

In Table II, the mean values for the transport of barium ion and water at the two concentrations are compared. The anode values are invariably the more reliable. With sodium chloride solutions this was found to be due to the tendency to the formation of alkali at the cathode. In the case of barium chloride, the low solubility of the hydroxide makes the error more difficult to correct. Therefore in Table II are included also the mean values of the above quantities calculated from anode results only. There is no significant difference between the two sets of values.

In view of the possibility of complex formation between the urea and the barium chloride, and also in order to obtain some information regarding the mobilities of the ions in the presence of urea, the effect of the latter on the molecular conductivity of barium chloride solutions of given volume concentrations was observed. The solutions were freshly made and were of about the same concentrations as those used in the main transport experiments.

TABLE II.

Temperature = 25° ± 0·02°.

	Mean of all values.		Mean of anode values.	
Concn.	0·25*M*.	0·5*M*.	0·25*M*.	0·5*M*.
$T_{\frac{1}{2}Ba}$	0·4056	0·3855	0·4008$_1$	0·3860$_5$
$T^H_{\frac{1}{2}Ba}$	0·4044	0·3822	0·3994$_9$	0·3813$_9$
n_w/n_s	0·305	0·434	0·345	0·612
n^F_w	0·124	0·166	0·136	0·234

The same conductivity cell (constant, 8·112) was used for all the solutions. No special precautions were taken for the attainment of extreme accuracy, as merely comparative results were required. The following table records the equivalent conductivities Λ_ϕ at 24·99° of approximately 0·25m_v and 0·5m_v-barium chloride in presence and in absence of 0·1*m*-urea, and the equivalent mobilities $U_{\frac{1}{2}Ba}$ and V_{Cl} of the barium and chlorine ion respectively, as calculated from the conductivities and the true transport numbers in the urea-containing solutions.

Concn.	Λ_ϕ.	$U_{\frac{1}{2}Ba}$.	V_{Cl}.	Concn.	Λ_ϕ.	$U_{\frac{1}{2}Ba}$.	V_{Cl}.
0·2501m_v-$BaCl_2$	88·22	—	—	0·5183m_v-$BaCl_2$	79·79	—	—
0·2501m_v-$BaCl_2$ + 0·1*m*-urea	87·82	35·20	52·62	0·5183m_v-$BaCl_2$ + 0·1*m*-urea	79·36	30·64	48·72

The reduction in conductivity due to urea is of about the same magnitude as that produced by urea in potassium chloride or sodium hydroxide solutions, in which cases it is ascribed to increase in viscosity (Fawsitt, *Z. physikal. Chem.*, 1904, **48**, 585; Chadwell and Asnes, *J. Amer. Chem. Soc.*, 1930, **52**, 3509). Since the urea, acting as a neutral medium in place of water molecules, increases the microscopic viscosity which opposes the movement of an ion in an electric field (Jones and Dole, *J. Amer. Chem. Soc.*, 1930, **52**, 2254), this assumption appears to be justified.

By making use of the densities of the solutions in question, the Hittorf transport numbers of the ions in each case can be compared with the corresponding values for solutions of barium chloride as determined by Jones and Dole (*loc. cit.*, 1929), and embodied in their empirical equation

$$t^H_{\frac{1}{2}Ba} = 1{\cdot}4476/(1 + 0{\cdot}0701\sqrt{c})$$

The required values are collected below.

Soln.	Concn. of soln., g.-mols./1000 g.	*d*, g./c.c.	Concn. of soln., g.-mols./l.	$T^H_{\frac{1}{2}Ba}$ ($BaCl_2$ + urea).	$T^H_{\frac{1}{2}Ba}$ (pure $BaCl_2$).
1	0·24056	1·04399	0·25114	0·3992	0·3985
4	0·47444	1·09235	0·51826	0·3811	0·3781

At each concentration the divergence between the Hittorf transport number in the pure barium chloride solution and in that containing urea is almost within the limits of experimental error, and the fact that the Hittorf transference number of the barium ion in the presence of urea is in each case slightly higher than in the pure salt solution emphasises the improbability of union between the barium ion and urea. This conclusion is supported by the spectroscopic investigations of Shibata, Inouye, and Natkatsuka (*Japanese J. Chem.*, 1922, **1**, 1), which indicate that even in 0·5*n*-salt solution, there is no complex formation between barium chloride and urea.

DISCUSSION.

It is of interest to compare the quantity of water n^F_w transported per faraday, the true equivalent transport number T_c, and the mobilities Λ_c for barium chloride solutions with the corresponding quantities for sodium chloride. These values are collected in Table III.

TABLE III.

Electrolyte.	Concn., g.-equivs./l.	T_c.	Λ_c.	n^F_w.	Electrolyte.	Concn., g.-equivs./l.	T_c.	Λ_c.	n^F_w.
NaCl	1·0	0·379	31·27	0·83	$BaCl_2$	1·0	0·386	30·55	0·234
	0·5	0·382	34·93	1·08		0·5	0·401	36·31	0·136

The values for sodium chloride at 0° which are not reproduced here are exactly analogous to the values at 25°, the increase in cathodic water transport on dilution being greater than at 25° (see Part II). In the case of sodium chloride the increase in the quantity of water

transported to the cathode both with decrease in concentration and with fall in temperature has been shown not to be entirely ascribable to change in the relative mobilities of ions which are carrying a fixed quantity of water. It therefore appears probable that with decreased concentration as well as with decreased temperature the number of water molecules carried by each ion increases.

The values for water transport recorded in Table III differ markedly for the two electrolyses: they are very much smaller for barium chloride, being of the order of 0·2 mole per faraday, as against approximately 1 mole for sodium chloride. Also, with decrease in concentration, a small increase in the transport number of the sodium ion accompanies considerable increase in water transport to the cathode, whereas in barium chloride solutions for the same concentration change, a five-fold greater increase in the cation transport number, $T_{\frac{1}{2}Ba}$ is accompanied by a slight decrease in water transport of about 0·1 mole per faraday.

These differences in behaviour may be referred to the bivalency of the barium ion. The electrostatic forces between the doubly charged ion and the surrounding water dipoles will be stronger than in the case of a singly charged ion—in fact, at least four times as great (see Gurney, "Ions in Solution," Cambridge, 1936). Consequently, at any concentration, the water molecules adjacent to the barium ion will be more firmly attached than in the case of the sodium ion, and the effect will be that of a permanent hydration shell. This accounts for the low mobility of the barium ion, which in spite of the double charge differs little from that of the sodium ion, being in the more concentrated solution slightly smaller, and in the more dilute solution slightly larger, than that of the sodium ion (Table III). On increase in the quantity of solvent, the mobilities of both anion and cation will be affected by two opposing influences, *viz.*, decrease in the restraint of the ionic atmosphere, and increase in the retarding load of water due to the larger number of water dipoles oriented round each ion; but the proportionate increase in the quantity of water associated with the already highly hydrated barium ion will probably be less than in the case of the chlorine ion, and we may expect an increase in the true transport number of the cation, not necessarily accompanied by an increase in cathodic water transport.

This is the phenomenon actually observed in the electrolysis of barium chloride as distinguished from sodium chloride, and it affords evidence of a hydration shell round the barium ion which is more permanent than that round the sodium or chlorine ion, in that it is not affected to the same degree by change in concentration of the solution.

On the other hand, it must not be forgotten that, according to the Debye–Onsager theory, among the neighbours of each ion there is a preponderance of ions of opposite sign which during the passage of a current are moving in the opposite direction and are carrying water with them. Each ion therefore moves in a medium which is not stationary but is streaming in the opposite direction. In any attempt to foretell the water transport, one would have in this connection to take account of the fact that the number of positive ions is only half that of the negative. We are at present without data for estimating the magnitude of this effect in concentrated solution, though it may possibly be an important factor in determining whether the water transport will increase or decrease for a given change in concentration.

There is no need to stress the observation that with increased dilution an increase in cation transport number is accompanied by a decrease in cathodic water transport. The experimental results indicate this relationship, but the largest weight of water actually transported in any single experiment was barely 0·19 g., *i.e.*, about 0·1% of the total weight of the electrode portion in which it was estimated. Consequently, the differences in the water transport in the two different dilutions will be almost within the limits of experimental error. The fact that a large rise in cation transport is not accompanied by a corresponding rise in cathodic water transport is sufficient to prove conclusively that, of the various factors affecting water transport, the decisive one is not a hydration shell of equal permanency and different magnitude attached to each ion.

Therefore, no significance can be attached to ionic hydration values calculated from the equation

$$n_w^T = (1 - n)m_k - nm_a \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$

where n_w^F is the number of g.-mols. of water transported per faraday, n is the true transport number of the anion, and m_a and m_k the number of water molecules assumed permanently attached to the anion and cation respectively.

Brintzinger and Ratanarat (*Z. anorg. Chem.*, 1935, **222**, 119; **223**, 103) have calculated total hydration values for a large number of ions, on the assumption of a hydration of 8 for the sodium and 4 for the potassium ion. These " standard " values are derived by applying equation (1) to the results of transport measurements in N-solution, a membrane having been used to separate the electrode portions (see Remy, *Fortschr. Chem.*, 1927, **19**, No. 2, 67; Baborovský and Wagner, *Z. physikal Chem.*, 1933, *A*, **163**, 132). Brintzinger's experiments consist in a comparison of the rates of dialysis of the ion under investigation and of the standard ion in $0{\cdot}1N$-solutions which are also $2N$ with regard to an alkaline nitrate. Since concentration has a considerable effect on water transport and on the hydration values calculated from it (Part I, *loc. cit.*), no reliance can be placed on values derived from standards which are almost certainly unreal and have been determined in conditions different from those under which the comparison is made. Schmitz-Dumont (*Z. anorg. Chem.*, 1935, **226**, 33) has adduced other evidence that Brintzinger's total hydration numbers have no physical basis; notwithstanding this, his values are quoted as being in exceptionally good accord with other properties of the ions (Tollert, *Z. physikal. Chem.*, 1935, *A*, **174**, 246).

Our results, with respect both to water transport and to the transference numbers of the ions, are at variance with the values recorded by Baborovský and Viktorin (*Coll. Czech. Chem. Comm.*, 1932, **4**, 155) for several concentrations of the salt. These investigators, using a membrane to separate the electrode portions, worked at temperatures varying from 19·5° to 24° and calculated a mean value both for water and for ion transport for each concentration over this temperature range. In all concentrations from **1·0** to $0{\cdot}2n$ they *observed transport of water to the anode, transport to the cathode being observed in* $0{\cdot}1n$-solution only.

Also, the Hittorf transport values $T^H_{\frac{1}{2}Ba}$ calculated from their ' true ' transport values and the water transport by means of Washburn's equation, $T_{\frac{1}{2}Ba} = T^H_{\frac{1}{2}Ba} + n^F_w n_s/n_w$, where n_s/n_w is the ratio of the number of equivalents of solute and water in the original solution, differ by about 20% from the values of Jones and Dole for the same concentrations. The available data (I.C.T., Vol. VI, p. 310; Jones and Dole, *loc. cit.*) show that the Hittorf transport numbers $T^H_{\frac{1}{2}Ba}$ in barium chloride solutions at 16° are only about 2% less than in the *same concentrations at 25°. There must therefore be some disturbing factor in the experiments* of Baborovský and Viktorin. Later experiments by these same authors (*Coll. Czech. Chem. Comm.*, 1933, **5**, 216), using the E.M.F. method for the determination of transport numbers, have shown that the presence of a separating membrane in approximately $0{\cdot}2m$-barium chloride solution reduces the barium transport number from 0·39 to 0·29, and that the decrease in cation transport becomes more marked with increasing concentration. This great decrease in transport number must be associated with a corresponding distortion of the water transport values. It is sufficient to account for the difference between our values and those of Baborovský and Viktorin, and emphasises the danger of using a membrane in transport measurements.

Summary.

Transport measurements have been carried out at 25° in $0{\cdot}5M$- and $0{\cdot}25M$-solutions of barium chloride containing $0{\cdot}1M$-urea as non-electrolytic reference substance. The water transport per faraday is found to be from one-quarter to one-eighth of that which occurs in sodium chloride solutions of equal equivalent concentrations. In both concentrations the water transport is to the cathode.

The Hittorf ionic transport numbers agree closely with those determined in the absence of urea by Jones and Dole. Both the Hittorf and true transport numbers of the barium ion show large increase with increasing dilution. Notwithstanding this, the cathodic water transport does not increase with increasing dilution. It is therefore suggested that the double charge on the barium ion produces a hydration shell which is more firmly bound and less sensitive to change in concentration than that round a chlorine or a sodium ion.

Neither the water nor the ion transport values agree with the corresponding values determined by Baborovský and Viktorin. The divergence is ascribed to the use of a membrane by these investigators.

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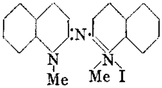
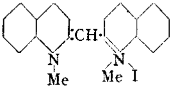
186. *Azacyanines.*

By NELLIE I. FISHER and FRANCES M. HAMER.

ALTHOUGH many varieties of cyanine dyes are known, there have only been two scientific publications giving preparative details of those related compounds in which one or more of the methenyl groups, which form the chain linking the heterocyclic nuclei, are replaced by one or more nitrogen atoms (Hamer, J., 1924, **125**, 1348; Fuchs and Grauaug, *Ber.*, 1928, **61**, 57). Patents making comprehensive claims with regard to substances of this type have recently appeared (Kendall, B.P. 447,038 and 447,109/1936; cf. *Proc. Ninth Int. Congr. Phot.*, 1936, 227), so that it seems desirable to place on record an account of independent work, in which certain compounds of this kind have been studied from a different angle.

Whereas the synthesis of 1 : 1′-dimethyl-2 : 2′-azacyanine * iodide (I) was a five-stage process, starting from 2-chloroquinoline and 2-aminoquinoline (Hamer, *loc. cit.*), the 2 : 2′-cyanine (II) was more simply prepared, by condensation of 2-iodoquinoline methiodide


(I.)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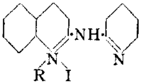
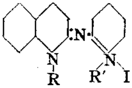

(III.)

with quinaldine methiodide (Fischer and Scheibe, *J. pr. Chem.*, 1920, **100**, 86), and this method proved capable of extension to the preparation of other types of 2′-cyanines (Hamer, J., 1928, 206; 1930, 995; Hamer and Kelly, J., 1931, 777; Fisher and Hamer, J., 1934, 1905; Brooker and Keyes, *J. Amer. Chem. Soc.*, 1935, **57**, 2488; Brooker, Keyes, and White, *ibid.*, p. 2492; Brooker, *ibid.*, 1936, **58**, 662).

The preparation of azacyanines has now been simplified, so that it has proved possible to prepare various types, for comparison with the appropriate 2′-cyanines. For instance, 2-iodoquinoline alkiodide was condensed with 2-aminopyridine to give 2-2′-*pyridylaminoquinoline alkiodide* (III). Removal of hydriodic acid, and treatment of the product with alkyl iodide, resulted in a 2-*pyrido*-2′-*azacyanine* (IV), three of which were prepared.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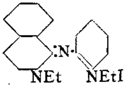
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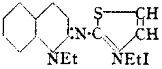

(VI.)

From 1-iodo*iso*quinoline ethiodide (Fisher and Hamer, J., 1934, 1905) and 2-aminopyridine, a 2-*pyrido*-1′-*azacyanine* (V) was synthesised, and, from 2-iodoquinoline ethiodide and 2-aminothiazole, a *thiazolo*-2′-*azacyanine* (VI).

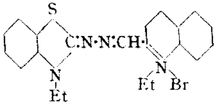
The absorption curve of a methyl-alcoholic solution of an azacyanine of each type was plotted, the diethyl compound being chosen in each instance. The maximum of the 2-pyrido-2′-azacyanine (IV; R = R′ = Et) lies 80 A. to the short wave-length side of that of the closely related 2-pyrido-1′-azacyanine (V). It has already been recorded that the principal absorption maximum of the 2 : 2′-azacyanine (I) lies 990 A. nearer to the region

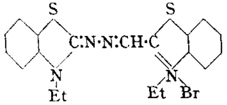
* Preferable to the original term "azocyanine."

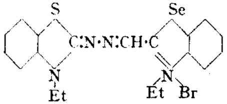
of short wave-length than does that of the 2 : 2′-cyanine (II) (Hamer, J., **1924**, **125**, **1348**). Two more values, 1020 A. and 700 A., respectively, are now obtained for the shift towards the blue caused by replacing by :N· the :CH· group, which links the nuclei in a 2′-cyanine: the former value by comparison of (IV) with 1 : 1′-diethyl-2-pyrido-2′-cyanine iodide, prepared from 2-iodopyridine ethiodide and quinaldine ethiodide by Hamer and Kelly (*loc. cit.*), the latter by comparison of (VI) with 3 : 1′-diethylthiazolo-2′-cyanine iodide, as recorded by Brooker, Keyes, and White (*loc. cit.*).

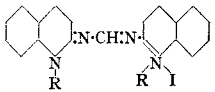
It should have been specified that the observation of one of us that the 2 : 2′-azacyanine (I) has no action on a photographic plate (Hamer, *loc. cit.*) was in fact confined to a gelatino-bromide plate; towards a gelatino-chloride plate it acts as a sensitiser, as noted by Kendall (*loc. cit.*). Of the three compounds represented by (IV), one confers a certain extra-sensitivity upon a gelatino-chloride photographic emulsion, but the other two extend the sensitivity so slightly that no maximum can be recorded. The 2-pyrido-1′-azacyanine (V) is without sensitising action, and the thiazolo-2′-azacyanine (VI) confers extra-sensitivity.

The method of Fuchs and Grauaug (*loc. cit.*) for preparing dyes, in which the two heterocyclic nuclei are linked by a three-membered chain :N·N:CH· (or ·N:N·CH:, since virtual tautomerism doubtless occurs in this series, as in the cyanines), consisted in condensing 2-ethylbenzthiazolonehydrazone, etc., with the aldehyde of the quaternary salt of a heterocyclic base, liberated from the corresponding *p*-dialkylaminoanil by the method of Kaufmann and Vallette (*Ber.*, 1912, **45**, 1736). The same method was followed in preparing

(VII.) 

 (VIII.)

(IX.) 

 (X.)

three new compounds (VII—IX) of this kind. By an extension of the nomenclature which has already been used, these compounds are designated as diazacarbocyanines. The positions of the nitrogen atoms in the three-membered chain are counted from that nucleus which is mentioned first. Thus (VII) represents an *αβ-diazathia-2′-carbocyanine*, (VIII) an *αβ-diazadithiacarbocyanine*, and (IX) a *βγ-diazaselenathiacarbocyanine*.

In (X), the three individual units of the chain joining the nuclei are the same as in (VII—IX), but they are arranged in a different order, :N·CH:N·. Two of these *αγ-diaza-2 : 2′-carbocyanines* have been prepared, by the action of ethyl orthoformate, in the presence of pyridine, on 2-aminoquinoline alkiodide, but the yields are much lower than those of the 2 : 2′-carbocyanines, obtained by reaction of ethyl orthoformate and pyridine with quinaldine alkiodide (Hamer, J., 1927, 2796).

With each of the three new dyes containing the chain :N·N:CH·, the principal absorption band of a methyl-alcoholic solution lies nearer to the region of short wave-length than does a secondary, ill-defined, band, whereas in true cyanines possessing a secondary absorption band, the reverse is usual (cf. Fisher and Hamer, *Proc. Roy. Soc.*, **1936**, *A*, **154**, 703). To determine the effect of replacing the carbocyanine chain, :CH·CH:CH·, by the chain :N·N:CH·, the positions of the maxima of the principal absorption bands were compared. Thus that of (VII) was compared with that of the thia-2′-carbocyanine, which has already been described by Ogata (*Bull. Inst. Phys. Chem. Res.*, **1934**, **13**, 556), and which we prepared by a different modification of the original method of I.C.I. Ltd., Piggott, and Rodd (B.P. 344,409/1929; B.P. 354,898/1930); the principal absorption maximum of (VIII) was compared with that which we have recorded for 2 : 2′-diethylthiacarbocyanine iodide (Fisher and Hamer, *loc. cit.*), and the maximum of (IX) with that of the selenathiacarbo-

cyanine, which we made for this purpose. With all three pairs, the compound with the chain :N·N:CH· was found to have its principal absorption maximum at a shorter wave-length than that of the compound with the chain :CH·CH:CH·, the values of the differences being 800, 770, and 820 A., respectively.

All the five original compounds of this αβ (or βγ)-diazacarbocyanine type were described by Fuchs and Grauaug as powerful photographic desensitisers. Of our new substances, (IX) is a powerful desensitiser, whilst (VII) and (VIII) considerably depress the original blue-sensitivity of a gelatino-bromide photographic emulsion, but at the same time confer a weak extra-sensitivity to green light. When the chain :N·N:CH· of (VII—IX) is replaced by :CH·CH:CH·, the resultant carbocyanines are, on the contrary, powerful sensitisers.

When the absorption maximum of compound (X) is compared with that which we have recorded for 1 : 1'-diethyl-2 : 2'-carbocyanine iodide, containing the chain :CH·CH:CH· (Fisher and Hamer, *loc. cit.*), the former is found to lie at a shorter wave-length, by 2620 A., than the latter. Thus in replacing the chain :CH·CH:CH·, the αγ-diazacarbocyanine chain has a much more powerful hypsochromic effect than has the αβ(or βγ)-diazacarbocyanine chain.

The diethyl compound (X; R = Et) depresses the blue sensitivity of a gelatino-bromide photographic emulsion, and weakly sensitises a chloride emulsion, whilst the dimethyl compound (X; R = Me) is photographically inert.

We have adopted a suggestion by Dr. F. Richter as to the desirability of inserting the systematic name of each cyanine described, as in the 1936 edition of Beilstein's "Handbuch der organischen Chemie." We are very grateful to Dr. Clarence Smith for his helpful consideration of, and discussion of, the nomenclature.

Experimental.

2-2'-Pyridylaminoquinoline Ethiodide (III; R = Et).—2-Iodoquinoline ethiodide (11 g.; 1 mol.) and excess of 2-aminopyridine (5 g.; 2 mols.) were boiled and stirred with absolute alcohol (50 c.c.) for 15 minutes, during which time solution occurred. The yellow crystalline product was ground with water and obtained in 46% yield (4·69 g.). After recrystallisation from water (200 c.c.) the yield was 38% (3·88 g.). A sample was dried in a vacuum at 80—100° and analysed by the method of Carius, which method of analysis was used throughout this work, except where otherwise stated (Found: I, 33·6. $C_{16}H_{16}N_3I$ requires I, 33·7%). M. p. 216°.

2-2'-Pyridylaminoquinoline methiodide (III; R = Me) was similarly prepared (64% yield) from 2-iodoquinoline methiodide and 2-aminopyridine; after extraction with ether, the residue was twice recrystallised from water (10 c.c. per g.) and obtained in 30% yield (Found in material dried at 80—100°: I, 34·9. $C_{15}H_{14}N_3I$ requires I, 34·95%). M. p. 206°, with softening from 202°.

1 : 1'-*Diethyl-2-pyrido-2'-azacyanine Iodide* (IV; R = R' = Et), or (1-*Ethyl-2-pyridine*)(1-*ethyl-2-quinoline*)*azamethincyanine Iodide*.—2-2'-Pyridylaminoquinoline ethiodide (5 g.; 1 mol.) and powdered crystalline sodium carbonate (7·6 g.; 2 mols.) were boiled with water (50 c.c.) for 15 minutes. The brown oil which separated was extracted with ether. After removal of the solvent from the dried extract, the oily residue was heated on the water-bath with ethyl iodide (1·3 c.c.; 1·2 mols.) for an hour. The resultant solid was washed with ether (4·16 g. obtained) and recrystallised from methyl alcohol (15 c.c.). The yield (3·25 g.) was 61%. The substance was dried in a vacuum at 60—80° and this method of drying was used except where otherwise stated (Found: I, 31·4. $C_{18}H_{20}N_3I$ requires I, 31·3%). M. p. 240°. The absorption maximum of a methyl-alcoholic solution of the pale yellow crystals lay at 3930 A.

1-*Methyl-1'-ethyl-2-pyrido-2'-azacyanine Iodide* (IV; R = Et, R' = Me), or (1-*Methyl-2-pyridine*)(1-*ethyl-2-quinoline*)*azamethincyanine Iodide*.—In an experiment similar to the preceding one, the oily base was heated with methyl iodide (1·2 c.c.; 1·2 mols.). After washing with ether, the pale yellow product (3·70 g.) was recrystallised from methyl alcohol (15 c.c.); the yield (3·2 g.) was then 61% (Found after a second recrystallisation: I, 32·4. $C_{17}H_{18}N_3I$ requires I, 32·5%). M. p. 232°.

1 : 1'-*Dimethyl-2-pyrido-2'-azacyanine Iodide* (IV; R = R' = Me), or (1-*Methyl-2-pyridine*)(1-*methyl-2-quinoline*)*azamethincyanine Iodide*.—2-2'-Pyridylaminoquinoline methiodide with sodium carbonate solution gave an oil, which with methyl iodide gave a 69% yield of the *aza-cyanine*. After recrystallisation from methyl alcohol (10 c.c. per g.), the yield of bright yellow product was 52% (Found: I, 33·6. $C_{16}H_{16}N_3I$ requires I, 33·7%). M. p. 258°. Upon a chloride emulsion it confers weak extra-sensitivity, with a maximum at 4250 A.

1 : 2′-*Diethyl-2-pyrido-1′-azacyanine Iodide* (V), or (1-*Ethyl-2-pyridine*)(2-*ethyl*-1-iso*quinoline*) *azamethincyanine Iodide*.—After 1-iodo*iso*quinoline ethiodide and 2-aminopyridine had been heated together in alcohol, ether precipitated an oil, which was heated with sodium carbonate solution. The product was taken up in ether and, after removal of the solvent from the dried extract, was heated with ethyl iodide. The yield was 19% after the yellow solid had been washed with ether, and 14% after it had been recrystallised from methyl alcohol (2 c.c. per g.) (Found : I, 31·7. Found after a second recrystallisation : I, 31·3. $C_{18}H_{20}N_3I$ requires I, 31·3%). The pale yellow product, m. p. 213°, gives an absorption maximum at λ3850 A.

3 : 1′-*Diethylthiazolo-2′-azacyanine Iodide* (VI), or (3-*Ethyl-2-thiazole*)(1-*ethyl-2-quinoline*)*azamethincyanine Iodide*.—2-Iodoquinoline ethiodide and 2-aminothiazole were condensed, the product treated with sodium carbonate, and the base obtained from it heated with ethyl iodide. After washing with ether, crystals were obtained in 20% yield and, after recrystallisation from methyl alcohol (10 c.c. per g.), in 16% yield (Found : I, 30·85. $C_{16}H_{18}N_3IS$ requires I, 30·9%). The bright yellow substance had m. p. 239°. Its absorption maximum is at λ3950 A. and it confers upon a chloride emulsion extra-sensitivity with a maximum at 4350 A.

2 : 1′-*Diethyl-αβ-diazathia-2′-carbocyanine Bromide* (VII), or (1-*Ethyl-2-quinoline*)(2-*ethyl*-1-*benzthiazole*)-*αβ-diazatrimethincyanine Bromide*.—The *p*-dimethylaminoanil of quinaldinealdehyde ethobromide (cf. Kaufmann and Vallette, *loc. cit.*) (1·99 g.; 1 mol.) was treated with cold dilute hydrochloric acid (8 c.c. of concentrated acid + 8 c.c. of water) and into the mixture was stirred 2-ethylbenzthiazolonehydrazone (Fuchs and Grauaug, *loc. cit.*) (1 g.; 1 mol.). The whole was boiled for 1 minute and then treated with a hot solution of sodium bromide (8 g.) in water (16 c.c.). The precipitated product was filtered off, washed with water, dried in a vacuum desiccator, powdered, and washed with ether. The undissolved residue (1·80 g.; 79% yield) was recrystallised from dilute methyl alcohol (50%; 4 c.c.), the yield then being 62% (1·42 g.) (Found : Br, 18·05. $C_{21}H_{21}N_4BrS$ requires Br, 18·1%). The brown crystals melted at 221° (decomp.). The principal absorption maximum of the methyl-alcoholic solution lies at λ4800, with an ill-defined weaker one at 5050 A. Whilst considerably depressing the blue sensitivity of a gelatino-bromide plate, the substance confers weak extra-sensitivity, which extends to 5800 A. for moderate exposures.

2 : 2′-*Diethyl-αβ-diazadithiacarbocyanine bromide* (VIII), or *bis*-(2-*ethyl*-1-*benzthiazole*)-*αβ-diazatrimethincyanine bromide*, was similarly prepared from the *p*-dimethylaminoanil of benzthiazole-1-aldehyde ethochloride (cf. Bloch and Hamer, *Phot. J.*, 1930, **70**, 374) and 2-ethylbenzthiazolonehydrazone. The washed product (67% yield) was recrystallised from dilute methyl alcohol (1·5 c.c. of methyl alcohol and 6 c.c. of water per g.), the yield then being 59%. It was recrystallised a second time before analysis (Found : Br, 17·6. $C_{19}H_{19}N_4BrS_2$ requires Br, 17·9%). M. p. 219° (decomp.), but shrinking began at *ca.* 120°. The brick-red substance has its absorption maxima in the same positions as has the preceding substance. It depresses the blue sensitivity of a photographic plate and confers weak green sensitivity, extending to 5700 A. for moderate exposures.

p-*Dimethylaminoanil of Benzselenazole-1-aldehyde Ethobromide*.—1-Methylbenzselenazole ethobromide (4 g.; 1 mol.), *p*-nitrosodimethylaniline (1·97 g.; 1 mol.), absolute alcohol (25 c.c.), and piperidine (4 drops) were boiled together for 3 hours. The product was filtered off, washed with ether, and recrystallised from methyl alcohol (22 c.c. per g.), being obtained in 26% yield (1·48 g.). Halogen in the presence of selenium was determined as described elsewhere (Hamer, *Analyst*, 1933, **58**, 26) (Found : Br, 17·6. $C_{18}H_{20}N_3BrSe,\frac{1}{2}CH_3{\cdot}OH$ requires Br, 17·6%). M. p. 225° (decomp., starting from 140°). The green crystals, when dissolved in methyl alcohol, give a broad absorption band, with its maximum at 5600 A. Like various other anils of this kind (Hamer, *Phot. J.*, 1929, **69**, 409; Bloch and Hamer, *loc. cit.*), the compound is a photographic desensitiser.

2 : 2′-*Diethyl-βγ-diazaselenathiacarbocyanine Bromide* (IX), or (2-*Ethyl*-1-*benzthiazole*)(2-*ethyl*-1-*benzselenazole*)-*αβ-diazatrimethincyanine Bromide*.—The washed product obtained (in 75% yield) from the above anil and 2-ethylbenzthiazolonehydrazone was recrystallised from methyl alcohol (13 c.c. per g.) and resulted in 30% yield (Found : Br, 16·15. $C_{19}H_{19}N_4BrSSe$ requires Br, 16·2%). The dull red crystals had m.p. 259° (decomp.). The principal absorption maximum is at 4800 A., with a weaker one at 5100 A. The substance possesses photographic desensitising properties.

2 : 1′-*Diethylthia-2′-carbocyanine Iodide*, or (1-*Ethyl-2-quinoline*)(2-*ethyl*-1-*benzthiazole*)*trimethincyanine Iodide*.—Ogata's method (*loc. cit.*) was to condense 2-β-anilinovinylquinoline ethiodide with 1-methylbenzthiazole ethiodide, in the presence of acetic anhydride and potassium acetate. In the present preparation, quinaldine ethiodide (4·98 g.; 1 mol.), 1-β-acetanilidovinyl-

benzthiazole ethiodide (7·5 g.; 1 mol.), anhydrous sodium acetate (1·5 g.), and acetic anhydride (36 c.c.) were boiled together for 1 hour. The product was filtered off and ground with ether and then with water (3·86 g.; 48% yield). A fractional crystallisation from methyl alcohol (100 c.c. × 3) effected the removal of the symmetrical 2 : 2'-carbocyanine in the last fraction, and the yield of pure dye from the first two fractions was 34% (2·73 g.) (Found: I, 26·2. Calc. for $C_{23}H_{23}N_2IS$: I, 26·1%). On heating, the green crystals lost solvent and melted at 248° (decomp.). Ogata gives m. p. 277°. The absorption maximum is at 5600 A.

2 : 2'-*Diethylselenathiacarbocyanine Iodide*, or (2-*Ethyl*-1-*benzthiazole*)(2-*ethyl*-1-*benzselenazole*)-*trimethincyanine Iodide*.—This was similarly prepared from 1-β-acetanilidovinylbenzselenazole ethiodide, 1-methylbenzthiazole ethiodide, sodium acetate, and acetic anhydride. The washed product (52% yield) was recrystallised from methyl alcohol (70 c.c. per g.) and thus obtained in 34% yield (Found: I, 23·3. $C_{21}H_{21}N_2ISSe$ requires I, 23·5%). The dull green crystals have m. p. 257° (decomp.). The absorption maximum lies at 5620 A.

1 : 1'-*Diethyl*-αγ-*diaza*-2 : 2'-*carbocyanine Iodide* (X; R = Et), or *Bis*-(1-*ethyl*-2-*quinoline*)-αγ-*diazatrimethincyanine Iodide*.—2-Aminoquinoline ethiodide (3 g.; 2 mols.), ethyl orthoformate (3·6 c.c.; 4 mols.), and pyridine (15 c.c.) were boiled together under reflux for 1 hour, after which the reaction mixture was treated with hot water (30 c.c.). The product obtained on cooling was filtered off, washed with water, and dried (0·80 g.; 33% yield). After recrystallisation from water (250 c.c.), the yield (0·60 g.) was 25%. It was dried for analysis in a vacuum at 80—90° (Found: I, 26·3. $C_{23}H_{23}N_4I$ requires I, 26·3%). The orange powder has m. p. 209°, with previous softening. The absorption maximum lies at λ3430 A. Its sensitising action on a chloride emulsion is very weak, with a maximum at 5000 A.

1 : 1'-*Dimethyl*-αγ-*diaza*-2 : 2'-*carbocyanine Iodide* (X; R = Me), or *Bis*-(1-*methyl*-2-*quinoline*)-αγ-*diazatrimethincyanine Iodide*.—The washed product (36% yield) similarly obtained from 2-aminoquinoline methiodide, ethyl orthoformate, and pyridine was recrystallised from water (270 c.c. per g.), being obtained in 17% yield. It was dried for analysis as in the preceding case (Found: I, 28·3. $C_{21}H_{19}N_4I$ requires I, 28·0%). The yellow powder melts at 193°.

We are deeply indebted to our colleagues Dr. E. P. Davey, Mr. R. B. Morris, and Dr. A. S. Roy for furnishing the absorption and sensitising data recorded in this paper.

KODAK LIMITED, WEALDSTONE, MIDDLESEX. [*Received, April 15th*, 1937.]

187. *Phthalocyanines. Part IX. Derivatives of Thiophen, Thionaphthen, Pyridine, and Pyrazine, and a Note on the Nomenclature.*

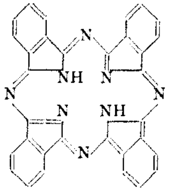
By R. P. LINSTEAD, E. G. NOBLE, and J. M. WRIGHT.

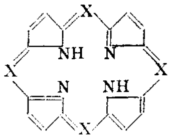
THIS and the three following papers are concerned with investigations of the chemistry of phthalocyanines in two main directions: (1) the possibility of obtaining similar compounds from heterocyclic instead of aromatic intermediates has been examined (Parts IX and X); (2) efforts have been made to bridge the gap between phthalocyanines and porphyrins.

The resemblance between these two groups has already been discussed (J., 1934, 1033; *Ann. Reports*, 1935, **32**, 359). The differences between the basic structures are two: phthalocyanine (*P*) contains four additional fused benzene rings and four linking nitrogen atoms in place of the four methene groups of porphin (*Q*, X = CH). To connect the two series more closely we have examined the possibility of preparing (*a*) compounds resembling phthalocyanine with nitrogen links but possessing no fused benzene rings (Part X), and (*b*) benzporphyrins, *i.e.*, analogous compounds with methene links and fused benzene rings (Part XI).

This extension of the field has created the need for a more precise nomenclature. The name phthalocyanine is now well established for compounds of the general type indicated by formula (*P*). It is proposed to use the term *porphyrazine* for the central ring system of the phthalocyanine molecule, that is, for the structure represented by formula (*Q*, X = N). Individual compounds are named by attaching an appropriate prefix. Thus the systematic name for phthalocyanine itself on this basis is tetrabenzporphyrazine and the corresponding compound with four pyridine rings in place of four benzenes becomes tetrapyridinoporphyrazine. To avoid undue complication it is not proposed to use the systematic names

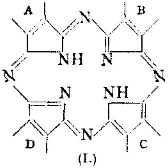
for simple phthalocyanines, but they have been employed in naming the heterocyclic compounds and derivatives of maleic acid in the papers which follow.

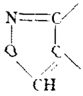
(P.) 

 (Q.)

On theoretical grounds it is to be anticipitated that there will be considerable differences in the ease with which phthalocyanine-like compounds are formed from *o*-dinitriles derived from various heterocyclic compounds. The most important factors which may be expected to influence the reaction are reviewed below.

(1) The common porphyrazine framework is represented in (I), where A, B, C and D indicate the position of four heterocyclic rings. This formula is not, however, fully adequate, as the molecule is in all probability a resonance hybrid between a number of similar structures, of which one is represented by formula (I), which is equivalent to the " Kekulé individuals " of aromatic chemistry. In this formula it will be seen that three of the heterocyclic corners (A, B and D) have to accommodate a double bond on the bridge and the fourth (C) an equivalent *o*-quinonoid arrangement. All the heterocyclic rings will not adapt themselves to such an arrangement with equal readiness, because the presence of the hetero-atom or atoms leads in many cases to a comparatively rigid, non-aromatic arrangement of double and single bonds. Thus pyridine is equivalent to benzene in this respect as in so many others, but *iso*oxazole (II) can only yield a compound of type (I) through the formation of a bridged form (III) :


(I.)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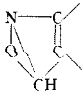
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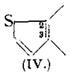
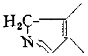
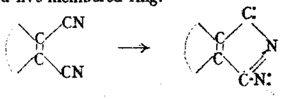

(IV.)

(V.)


(VI.)

Moreover, in many heterocyclic rings the various pairs of *o*-carbon atoms are not equivalent. Thus the thiophen (or furan) ring may be simply fused to formula (I) in the 2 : 3-position (IV), but for fusion in the 3 : 4-position (V), bridging of the thiophen ring is necessary. In the pyrrole ring another type of adjustment is possible, for a 3 : 4-derivative can adapt itself by migration of hydrogen, as in (VI), as well as by bridging. It is reasonable to suppose that bridged structures, such as (III), will have very much lower stabilities than the corresponding unsaturated structures, such as (II). Hence there will be little possibility of resonance and a departure from the aromatic type. On these grounds it is to be expected that phthalocyanine-like compounds will not be formed from such heterocyclic rings, or if capable of existence, will be comparatively unstable.

(2) As one fundamental stage in the formation of porphyrazines is the cyclisation (VII) ⟶ (VIII), it will be affected by the ease with which the heterocyclic system yields *o*-derivatives containing a five-membered ring.

(VII.)  (VIII.)

A convenient practical guide is provided by the capacity of the corresponding *o*-dicarboxylic acids and their diamides to yield respectively anhydrides and imides. There are large differences between heterocyclic compounds in this respect. For example, as far as our present knowledge goes, anhydrides are readily formed in the pyridine, pyrazine and thiophen series, with difficulty in the pyrrole and (3 : 4-)furan group, and not at all from *iso*oxazole (3 : 4-) and triazole compounds (see table).

(3) It is obvious that the formation of porphyrazines will only proceed in the absence of side reactions. The most dangerous of these is gross thermal decomposition, but other side reactions may originate at the hetero-atom; for example, the acidity of the imino-hydrogen atom in pyrrole and particularly in triazole derivatives may lead to combination with the metallic reagents used for the preparation of the porphyrazines.

To summarise: the formation of porphyrazines from heterocyclic compounds may be expected when (i) they contain the arrangement (VII) or are capable of yielding this arrangement easily; (ii) they possess the necessary thermal stability and no disturbing reactive centre in the heterocyclic ring; and (iii) when the heterocyclic system is capable of yielding *o*-five-membered rings.

The formation of porphyrazines from the ten heterocyclic systems mentioned in the table has been investigated by the authors and Dr. J. A. Bilton. Column 2 gives the rearrangement (if any) necessary in the heterocyclic ring to accommodate porphyrazine formation. Column 3 indicates the tendency of the *o*-dicarboxylic acid of the series or its amide to yield cyclic derivatives (anhydride, imide).

Ring.	Rearrangement.	Ortho-ring formation.
Thiophen 2 : 3	None	Easy [1]
Thionaphthen 2 : 3	None	Easy [1]
Furan 3 : 4	Bridging	Difficult [3]
Pyridine 2 : 3	None	Easy [1, 2]
Pyrazine 2 : 3	None	Easy [1]
Pyridazine 4 : 5	None	Fairly easy [1]
Pyrrole 2 : 3	None	Very difficult [4]
Pyrrole 3 : 4	Bridging or H migration	Very difficult [4]
*iso*Triazole	None	Apparently impossible [5]
*iso*Oxazole	Bridging	Apparently impossible [1]

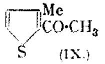
[1] See present work. [2] Engler, *Ber.*, 1894, **27**, 1788; Gabriel and Colman, *Ber.*, 1902, **35**, 2842, etc. [3] Anhydride and imide formed when the furan ring contains phenyl substituents, but not when it contains methyl substituents (Seka, *Ber.*, 1925, **58**, 1783). [4] No imides and only two anhydrides known (Piloty, *Annalen*, 1915, **407**, 5; Seka, *loc. cit.*). [5] Anhydride and imide formation apparently impossible (Fries, *Annalen*, 1927, **454**, 121, correcting earlier work by v. Pechmann, *Annalen*, 1896, **262**, 311, and Beretta, *Gazzetta*, 1926, **55**, 790).

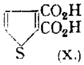
It follows from the theory outlined above that porphyrazines should be formed in the following series: thiophen (2 : 3), thionaphthen, pyridine, pyrazine, and probably pyridazine. We should not expect to obtain similar products from the corresponding furan, or *iso*oxazole derivatives, and the other three systems are doubtful.

Actually, coloured substances closely resembling phthalocyanines were obtained in the thiophen (2 : 3), thionaphthen, pyridine, and pyrazine series. Definite negative evidence was obtained in the pyrrole (3 : 4), *iso*oxazole, and *iso*triazole series. The other systems gave no positive results, but the negative results cannot be taken as conclusive, as none of the necessary *o*-dinitriles could be obtained. The present paper describes the four groups of compounds which yielded positive results. The work in the other series is described in Part X (following paper).

Preparation of Intermediates.—In the thiophen, thionaphthen and pyridine series, the general procedure followed that used for the preparation of phthalocyanines. The *o*-dicarboxylic acid, corresponding to phthalic acid, or its anhydride, was converted into the dinitrile or the *o*-cyanoamide. The starting material in the thiophen group was 3-methylthiophen; this is acetylated in the 2-position to give a ketone (IX) which can be oxidised to thiophen-2 : 3-dicarboxylic acid (X) (Demuth, *Ber.*, 1885, **18**, 3024; Gerlach, *Annalen*, 1892, **267**, 145). Actually we found that acetylation also occurred to a minor extent in the 5-position, so that the dicarboxylic acid contained the 2 : 4(= 3 : 5)-acid (XI) as impurity. Of the two acids, only the 2 : 3-acid yielded an anhydride, in agreement with the orienta-

tions given in the literature. The 2 : 3-acid was converted into the *dinitrile* by the methods described in the experimental section.


(IX.)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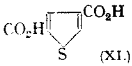
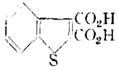

(XI.)

Attempts to prepare thiophen-3 : 4-dicarboxylic acid from 3 : 4-dimethylthiophen and 2 : 5-dimethylthiophen-3 : 4-dicarboxylic ester from diacetylsuccinic ester were unsuccessful. The 3 : 4-series could not therefore be examined; this was unfortunate, as it would have given useful information as to the importance of the bridging effect.

The parent acid (XII) of the thionaphthen series was easily prepared from thioindoxyl, and the dinitrile obtained without much difficulty. On the other hand, although pyridine-2 : 3-dicarboxylic acid (quinolinic acid, XIII) was readily obtainable by the oxidation of 8-hydroxyquinoline, its dinitrile could not be obtained. The corresponding cyanoamide was, however, prepared and yielded phthalocyanine-like compounds.

In the pyrazine series the dinitrile was available without the intervention of the corresponding acid. Grischkevitsch-Trochimovski (*Rocz. Chem.*, 1928, **8**, 165) has shown that the tetrameride of hydrogen cyanide, reacting as diaminomaleinitrile (XIV), condenses with glyoxal to yield 2 : 3-dicyanopyrazine (XV). The structure of the product was established by hydrolysis to the corresponding acid and decarboxylation to pyrazine, although no detail was given of the method of identification of the base. In the present work we have confirmed this by hydrolysis to pyrazinemonocarboxylic acid (XVI), identified by direct comparison with material synthesised by the method of Gabriel and Sonn (*Ber.*, 1907, **40**, 4850). The formation of dicyanopyrazines in this way appears to be a general reaction of 1 : 2-diketones, comparable with the formation of quinoxalines. It occurs with diacetyl, benzil, and phenanthraquinone.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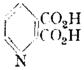
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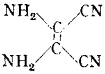
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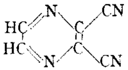
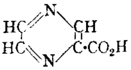
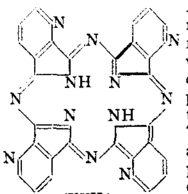

(XV.)


(XVI.)

Preparation of Porphyrazines.—The 2 : 3-dicyano-derivatives of thiophen, thionaphthen and pyrazine, and the 2 : 3(or 3 : 2)-cyanoamide derived from pyridine all yielded blue to green compounds when heated with suitable metallic reagents. The identification of these as the heterocyclic analogues of phthalocyanines followed from their general resemblance in physical and chemical properties, elementary composition, and absorption spectra (unpublished work by Dr. E. F. Bradbrook). The copper derivatives were prepared in all four series and also the metal-free compounds derived from thionaphthen, pyridine and pyrazine. As in the phthalocyanine group, copper was firmly held in these complexes, but magnesium was displaced by treatment with sulphuric acid and precipitation with water. The three metal-free compounds were obtained in this way.

A number of difficulties were encountered in the purification of these compounds. Although fairly stable to heat, they lacked the outstanding resistance of phthalocyanines, and none could be sublimed satisfactorily. Several partly decomposed on prolonged extraction with high-boiling solvents and in only one case could a macrocrystalline product be obtained. This was probably due to the presence of structural isomerides, similar to those found among the naphthalocyanines (Bradbrook and Linstead, J., 1936, 1744). The isomerism depends upon the relative positions of the heteroatoms and can be easily visualised for tetra-2 : 3-pyridinoporphyrazine, one form of which is shown in formula (XVII). This does not apply to the tetrapyrazinoporphyrazines, which can only exist in one form, but purification of this group was difficult owing to the formation of hydrates. As a result of these difficulties, the analytical figures


(XVII.)

were not entirely satisfactory, but showed a general agreement with the type $[R(CN)_2]_4$Met. or $[R(CN)_2]H_2$, where R represents the heterocyclic residue and Met. a bivalent metal.

Apart from the general fall in stability, the most interesting difference between tetra-2 : 3-pyridinoporphyrazine (XVII) and phthalocyanine is that the pyridine derivative forms a *dimethiodide* and is soluble in comparatively dilute sulphuric acid. Both these reactions may be attributed to salt formation at the nitrogen atoms of the pyridine rings.

EXPERIMENTAL.

Thiophen Series.

By the method of Higson and Thorpe (J., 1906, **89**, 1462) 135 g. of ethyl cyanoacetate and 87·5 g. of acetaldehyde cyanohydrin yielded 134 g. of α-methylsuccinic acid. The following modification of Bone and Sprankling's process (J., 1899, **75**, 852) was found to be rather more convenient for the routine preparation of large quantities. The sodium compound from 143 g. of cyanoacetic ester and a solution of 28·8 g. of sodium in 350 c.c. of alcohol was treated slowly with 210 g. of ethyl α-bromopropionate. At the end of the spontaneous reaction, the mixture was heated until neutral (about ½ hour), and the methyl cyanosuccinic ester isolated in the usual way. Yield, 185 g. of a fraction, b. p. 160—165°/17 mm. The ester was boiled with 8 vols. of concentrated hydrochloric acid for 6 hours, and the product evaporated to dryness. The powdered residue was exhaustively extracted with acetone (Soxhlet). Evaporation of the extract yielded α-methylsuccinic acid, m. p. 107—109°, in 80—85% yield. The sodium salt was prepared from this acid by exact neutralisation, dried in a vacuum at 180—200°, and converted into 3-methylthiophen by fusion with phosphorus trisulphide (Volhard and Erdmann, *Ber.*, 1885, **18**, 455). With the object of improving the low and erratic yields obtained in this reaction various modifications were introduced (see table) but without much success. The best results appear to be obtained by slow initial heating. The yields given are those of material purified by refluxing over sodium and redistillation, b. p. 116—120°.

Expt.	Sodium salt, g.	P_2S_3, g.	Procedure.	Yield.
1	92	140	Rapid initial heating	9·5 g.; 18%
2	100	150	As (1) in a stream of CO_2	12 g.; 22%
3	200	250	Slow initial heating	34 g.; 30%
4	200	250	,, ,,	22 g.; 20%
5	235	295	,, ,,	37 g.; 28%
6	220	275	As (3), mixture diluted with sand	22 g.; 18%

On treatment with acetyl chloride following Demuth and Gerlach (*locc. cit.*) 3-methylthiophen gave consistently good yields (75—80%) of 2-acetyl-3-methylthiophen (IX), b. p. 98—104°/13 mm. Subsequent experiments showed this to contain a little of the 5-acetyl isomeride as impurity.

Oxidation of this ketone (cf. Gerlach, *loc. cit.*) was examined in detail, the following being a typical result: 195 g. of powdered potassium permanganate were added during 90 minutes to a mechanically stirred emulsion of 35 g. of 2-acetyl-3-methylthiophen in 2100 c.c. of water containing 280 g. of caustic soda. The reaction was complete after another hour's stirring and 2 hours' heating on the steam-bath. The liquid was filtered hot, evaporated to one-third of its bulk, acidified, and extracted six times with ether (further continuous extraction with ether yielded only oxalic acid, 4 g.). The united hand extracts yielded 24 g. of solid product, which was roughly separated by trituration with cold benzene. The soluble material (12 g.) was impure 3-methylthiophen-2-carboxylic acid (Gerlach, *loc. cit.*). The portion insoluble in benzene was separated by fractional crystallisation from water into 5 g. of thiophen-2 : 3-dicarboxylic acid (X), which formed stout prisms, m. p. 270° (Found: S, 18·5. Calc. for $C_6H_4O_4S$: S, 18·6%), and 0·8 g. of thiophen-2 : 4-dicarboxylic acid (XI), which crystallised in tufts of needles, m. p. 280° (Found: S, 18·4%). These were identified by conversion into the dimethyl esters through the silver salts. The m. p. of the 2 : 3-ester was 58° (Gerlach, *loc. cit.*, gives 60°); that of the 2 : 4-ester was 120° (Zelinsky, *Ber.*, 1887, **20**, 2017, gives 121°). The aqueous mother-liquors from these dicarboxylic acids yielded oxalic acid dihydrate (equiv., 63; m. p. and mixed m. p. 102°).

The effect of minor variations in the experimental conditions of the oxidation on the yield and nature of the products is shown in the table. The ease with which the monocarboxylic acid is formed without oxidation of the methyl group is indicated by experiment (3).

Expt.	Ketone, g.	Alkali, g.	Water, l.	Permanganate, g.	Yield, monocarboxylic acid, g.	Yield, dicarboxylic acid, g.
	5	4	0·3			
1	35	280	2·1	195	12	5·8
2	32	265	3	176	10·2	6
3	96	600	6	516	56	1
4	45	360	3·6	246	20	8
5	32	350	2	176	7	3

3-Methylthiophen-2-carboxylic acid, when once formed, resisted all attempts at oxidation to the dicarboxylic acid, the only isolated product being oxalic acid.

Oxidation of Thionaphthen.—Attempts were made to prepare thiophen-2 : 3-dicarboxylic acid by the direct oxidation of thionaphthen. Thioindoxyl was separated from the commercial melt of phenylthioglycollic-*o*-carboxylic acid by acidification with concentrated hydrochloric acid at 90° in an atmosphere of carbon dioxide. The product was reduced with zinc dust in boiling acetic acid, and the thionaphthen isolated by neutralisation and distillation in steam, m. p. 32° (cf. Friedländer, *Ber.*, 1908, **41**, 230). Thionaphthen was oxidised under the conditions tabulated below. The liquid was filtered, cleared with sulphur dioxide, and extracted exhaustively with ether.

Thionaphthen, g.	Permanganate, g.	Alkali.	Water, c.c.	Conditions.
7	47	60 g. NaOH	500	2 Hours at b. p.
5	34	50 g. NaOH	500	4 Days at 80° with 500 c.c. of acetone.
5	34	None	500	4 Days at 80°.
7	45	60 g. NaOH	700	2 Weeks at 35°.
4·5	35	9 g. $CaCO_3$	900	Compare the preparation of pyridine-2 : 3-dicarboxylic acid, p. 918.

In no case was any organic acid, soluble in ether, isolated; nor could the presence of sulphonic or sulphinic acid be detected. Sulphate was present in the original oxidation product, before the addition of sulphur dioxide. Hence such thionaphthen as is not recovered unchanged with the manganese dioxide is completely oxidised under these experimental conditions.

Derivatives of Thiophen-2 : 3-dicarboxylic Acid.—The pure acid (4·5 g.) was refluxed for 30 minutes with 16 c.c. of acetic anhydride, the cooled product poured into 500 c.c. of water, and the precipitate of *anhydride* filtered off, dried, and crystallised from benzene; m. p. 140°, yield 3·6 g. (Found: S, 20·4. $C_6H_2O_3S$ requires S, 20·7%). The anhydride could also be made by similar treatment of the mixed dibasic acids (insoluble in benzene) obtained from the oxidation of acetyl-3-methylthiophen. The 2 : 4-acid separated slowly from the residual solution after removal of the 2 : 3-anhydride. This difference confirms the orientation of the carboxyl groups in these acids. The anhydride sublimed in poor yield when the 2 : 3-acid was heated in a current of nitrogen or, better, at 2 mm. pressure. It was not formed by the action of a mixture of phosphorus pentachloride and oxychloride on the acid.

Thiophen-2 : 3-dicarboxylic acid (7·5 g.) was refluxed for 18 hours with 25 c.c. of thionyl chloride and 17 c.c. of dry benzene. The excess of reagent was removed under diminished pressure, the residual acid chloride dissolved in 100 c.c. of dry benzene, and the solution saturated with dry ammonia for ½ hour. The precipitated *diamide* crystallised from water in needles, m. p. 228°. Yield, 4 g. (53%) (Found: N, 16·5. $C_6H_6O_2N_2S$ requires N, 16·5%). Acidification of the mother-liquor from the diamide yielded 2 g. of a white flocculent precipitate of the corresponding amic acid (2 : 3- or 3 : 2-), m. p. 238°, soluble in sodium bicarbonate solution. The amic acid on dehydration at 230—240° with phosphoric oxide yielded 1 g. of the *imide* of thiophen-2 : 3-dicarboxylic acid as a crystalline sublimate, m. p. 204° (Found: N, 9·0. $C_6H_3O_2NS$ requires N, 9·1%). The structure of this followed from the fact that it gave the diamide (m. p. 228°) in good yield after standing overnight with aqueous ammonia (*d* 0·880). A mixture of diamide and amic acid was also formed, but in worse yield, by treating the anhydride with phosphorus pentachloride, removing the phosphorus oxychloride, and treating the acid chloride in the manner described above.

An intimate mixture of 9 g. of the diamide and 15 g. of phosphoric oxide was heated in a special apparatus, which was found convenient for the distillation and sublimation of unstable solids. This consisted of a vertical tube, fitted with a wide horizontal side-arm, and enclosed in a fused-on outer jacket containing a suitable heating liquid. At a bath temperature of 180—190° and 3 mm. pressure, the above mixture gave a distillate, b. p. 130—135°, which immediately

solidified in the side-arm. The crude product (3·2 g., m. p. *ca.* 120°) was 2 : 3-*dicyanothiophen* contaminated with about 20% of imide (Found : N, 18·5%). The mixture was kept overnight in aqueous ammonia (*d* 0·880), and the solid filtered off and extracted with acetone. Evaporation of the acetone extract left the dinitrile, which formed needles from light petroleum, m. p. 140° (Found : N, 20·3. $C_6H_2N_2S$ requires N, 20·9%). Dehydration of the diamide with acetic anhydride also yielded crude dinitrile, but in worse yield.

The dinitrile (1·7 g.) was heated at 230—250° with 1·4 g. of cuprous chloride for about 10 minutes, the mixture becoming solid. The product was powdered and exhaustively extracted with boiling alcohol. The blue residue was dusted into concentrated sulphuric acid, and the brown solution filtered through asbestos and poured on ice. The greenish-blue precipitate was washed and dried (1·1 g.) and twice crystallised from chloronaphthalene by the usual technique. This procedure was wasteful, as even exhaustive extraction left a considerable residue (which gave a fine blue solution in quinoline) and as a good deal of the soluble pigment failed to separate from the chloronaphthalene.

Copper tetra-2 : 3-*thiophenoporphyrazine* separated as a greenish-blue powder with a faint purple lustre (Found : C, 47·7; H, 1·8; S, 19·4; Cu, 9·6. $C_{24}H_8N_8S_4Cu$ requires C, 48·0; H, 1·7; S, 21·3; Cu, 10·6%). The substance was greener than free phthalocyanine and resembled zinc phthalocyanine hydrochloride. It could not be sublimed under the conditions normally used for phthalocyanines. A similar compound appeared to be formed from 2 : 3-dicyanothiophen and metallic copper, but the nitrile gave no obvious signs of pigment formation when heated with sodium amyloxide, litharge, or magnesium.

3 : 4-*Thiophen Series*.—(*a*) Ethyl methylcyanosuccinate (160 g.) was methylated following Bone and Sprankling (*loc. cit.*), and the dimethylated ester (133 g.) hydrolysed with 6 volumes of boiling concentrated hydrochloric acid for 20 hours. The solution was evaporated to dryness, and the αβ-dimethylsuccinic acid extracted with acetone. Dry distillation of a mixture of 195 g. of the sodium salt of this acid (dried at 200°) and 245 g. of phosphorus trisulphide in a stream of carbon dioxide yielded 83 g. of crude dimethylthiophen. This was left in contact with sodium hydroxide for 15 hours, refluxed over sodium for 6 hours, and fractionated. Yield of 3 : 4-dimethylthiophen, b. p. 145—148°, 50 g. (compare Zelinsky, *Ber.*, 1888, **21**, 1836). Oxidation of this substance with alkaline permanganate under a variety of conditions yielded mainly oxalic acid, a small amount of 3-methylthiophen-4-carboxylic acid, and no thiophen-3 : 4-dicarboxylic acid.

(*b*) Diacetylsuccinic ester (Knorr, *Ber.*, 1894, **27**, 1155) yielded only a black pitch when refluxed with 1·5 parts of phosphorus pentasulphide in 5 parts of toluene for one hour. When 5 g. of the ester were refluxed for 90 minutes with 1·7 g. of phosphorus pentasulphide in 25 c.c. of anhydrous benzene, some hydrogen sulphide was evolved, but after filtration of the unattacked sulphide, evaporation of the solvent led to a good recovery of the ester and no other isolable product.

Thionaphthen Series.

Thionaphthenquinone (33 g., m. p. 118—119°) was prepared from thioindoxyl (43 g.) essentially by Mayer's method (*Annalen*, 1931, **488**, 259) and was converted into thionaphthen-2 : 3-dicarboxylic acid (XII) following Friedländer (*Ber.*, 1908, **41**, 227). Yield 75% of needles, m. p. 255°. The acid gave an excellent yield of anhydride, m. p. 173°, when boiled for ½ hour with 3 volumes of acetic anhydride (cf. Mayer, *loc. cit.*).

The anhydride (15 g.) was heated with phosphorus pentachloride (12 g.) for 6 hours at 150—160°. The acid chloride (m. p. 70—72°) separated partly on standing and partly after removal of phosphorus oxychloride. Yield, 18 g. (90%). It was dissolved in anhydrous benzene and treated with dry ammonia gas. The white precipitate of *thionaphthen*-2 : 3-*dicarboxyamide* was crystallised from water. Yield 2 g., m. p. 204—205° (Found : N, 12·9. $C_{10}H_8O_2N_2S$ requires N, 12·7%). Acidification of the aqueous mother-liquor from this yielded 2 g. of a white solid, presumably the amic acid. This on distillation with phosphoric oxide yielded *thionaphthen*-2 : 3-*dicarboxyimide*, which crystallised from acetic acid in small plates, m. p. 240° (Found : N, 7·2. $C_{10}H_5O_2NS$ requires N, 6·9%). When treated with an excess of aqueous ammonia (*d* 0·880), the imide gave a quantitative yield of the diamide, m. p. 204°. Experiments on the preparation of the acid chloride from the acid and thionyl chloride were unsatisfactory. The principal product was the anhydride, m. p. and mixed m. p. 173°. Preliminary experiments on the preparation of the imide by melting the anhydride with ammonium carbonate and with urea also gave unpromising results.

Thionaphthen-2 : 3-dicarboxyamide (2 g.) was refluxed for 1 hour with 6 c.c. of acetic

anhydride (6 mols.). The product was cooled and poured into water. The precipitated 2 : 3-*dicyanothionaphthen* (1·5 g.) was crystallised from alcohol to a constant m. p. of 148° (1·2 g.) (Found : N, 14·9. $C_{10}H_4N_2S$ requires N, 15·2%). Similar yields of 80—85% were obtained on a larger scale. When 5 g. of the diamide were dehydrated by 30 minutes' refluxing with 5 c.c. of acetic anhydride and an equal volume of acetic acid, the product (4·5 g.) was 2(or 3)-*cyanothionaphthen*-3(or 2)-*carboxyamide*, which crystallised from alcohol in long needles, m. p. 192—194° (Found : N, 13·7. $C_{10}H_6ON_2S$ requires N, 13·9%). This yielded green pigments when heated with cuprous chloride, reduced copper and, less readily, with magnesium. An intimate mixture of 1 g. of the diamide and 1 g. of phosphoric oxide was heated at *ca.* 1 mm. in the special apparatus already described. Reaction commenced at about 220° and the bath temperature was maintained at 230—240° until nothing further sublimed and the charred residue began to swell; 0·4 g. (*ca.* 70%) of solid was removed from the side-arm. This melted at about 195° and was a mixture of dinitrile and imide (Found : N, 9·8%). Separation was difficult, treatment with ammonia (cf. p. 917) being unsatisfactory. Repeated extraction with cold ether, alcohol, or benzene led to an accumulation of imide in the less soluble fraction and this was finally crystallised from acetic acid; it then melted at 238° and was identical with that already described. The purest dinitrile which could be isolated from the soluble portion melted at 140—145° and contained 14·0% of nitrogen (Calc., 15·2%).

Tetra-2 : 3-*thionaphthenoporphyrazines*.—A mixture of 1 g. of 2 : 3-dicyanothionaphthen and 0·5 g. of cuprous chloride was heated at 240—250° for 30 minutes, and the product cooled, powdered, and exhaustively extracted with alcohol to remove unreacted nitrile. The dark green residue was dissolved in concentrated sulphuric acid (blue solution), precipitated in the usual way, washed with water until free of acid, and finally washed with alcohol. The product (0·5 g.) was extracted with chloronaphthalene (green solution), from which it separated as a dull green powder with a faint purple lustre. The colour was slightly duller than that of 1 : 2-naphthalocyanine (Found for once crystallised material : C, 58·1; H, 2·3; N, 12·9; S, 15·4. Found for twice crystallised material : C, 58·7; H, 1·8; N, 12·3; S, 15·2. $C_{40}H_{16}N_8S_4Cu$ requires C, 60·0; H, 2·0; N, 14·0; S, 16·0. $C_{40}H_{15}N_8ClS_4Cu$ requires C, 57·5; H, 1·9; N, 13·4; S, 15·3%). The last of these sets of figures corresponds with the substitution of chlorine for one nuclear hydrogen as in copper monochlorophthalocyanine (Dent and Linstead, J., 1934, 1027). As in the thiophen series, the extraction was inefficient and the product from sulphuric acid treatment appeared to be a mixture of substances of closely similar type. A portion was undissolved even by prolonged extraction with chloronaphthalene at 260°, but dissolved in sulphuric acid and yielded a green precipitate on dilution. A considerable amount of the soluble portion failed to separate from the chloronaphthalene. A similar preparation using reduced copper in place of cuprous chloride gave a product indistinguishable from the above (Found : C, 57·8; H, 1·9; N, 12·2; S, 15·1%). Reaction between the 2 : 3-cyanoamide (m. p. 193°, 2 g.) and reduced copper (1·25 g.) proceeded vigorously at 240—250°. The dark green product, worked up as before, was purified through sulphuric acid (yield, 1·3 g.) and showed a similar lack of homogeneity when extracted with chloronaphthalene.

2 : 3-Dicyanothionaphthen reacted smoothly with aluminium chloride at 250° to give a dark green pigment, soluble in chloronaphthalene and slightly soluble in alcohol (green solution). The solution in concentrated sulphuric acid was dark olive-green and yielded a green precipitate on dilution, the colour of which was unchanged by alkali. The dinitrile reacted readily with etched magnesium at 250° to give a dark green pigment partly soluble in ether, like α-magnesium 1 : 2-naphthalocyanine (Bradbrook and Linstead, *loc. cit.*). Three days' extraction with ether (Soxhlet) separated the product into a soluble portion (ash, 4·9%. Calc., for magnesium tetrathionaphthenoporphyrazine, 5·3%) and an insoluble portion (ash, 4·5%) which were indistinguishable in appearance. The insoluble portion dissolved in sulphuric acid with an olive-green colour, and the solution gave a dark green precipitate of metal-free compound on dilution (ash, 0·4%).

Pyridine Series.

Pyridine-2 : 3-dicarboxylic (quinolinic) acid (XIII) was prepared by the oxidation of quinoline (compare G. P. 414,072) and, better, of 8-hydroxyquinoline (Sucharda, *Ber.*, 1925, **58**, 1727). The direct oxidation of the base gave indifferent yields in spite of a large number of modifications. The following experiments are typical. (*a*) 10 G. of quinoline were gradually added to a mechanically stirred solution of 82 g. of potassium permanganate in 2 l. of water containing 20 g. of calcium carbonate. After 15 hours' stirring, the solution was filtered, evaporated to a syrup, acidified with nitric acid, neutralised, and treated with silver nitrate until there was no further

precipitate. The precipitate was washed, dried (35 g.), and refluxed for 48 hours with 30 c.c. of ethyl iodide and 600 c.c. of dry ether. The ester was fractionated into 5 g. of ethyl oxalate, b. p. 80°/15 mm., and 4 g. of ethyl quinolinate, b. p. 170—180°/15 mm. The ethyl oxalate was identified by conversion into oxamide (Found: N, 32·1. Calc., 31·9%). The use of barium carbonate in place of calcium carbonate gave a similar result. Variation in the concentration had little effect, and in an experiment on a much larger scale (500 g. of quinoline) the proportion of ethyl oxalate to quinolinate in the product rose to *ca.* 10 : 1. (*b*) Process (*a*) was followed except that lead nitrate was used in place of silver nitrate. The powdered dry lead salt (33 g.), suspended in 100 c.c. of water, was treated at 60° with a rapid stream of hydrogen sulphide. The lead sulphide was filtered off and washed thoroughly with boiling water. The filtrate yielded 5 g. of oxalic acid on evaporation to small bulk, and 1 g. of quinolinic acid separated from the washings. (*c*) By Sucharda's process (*loc. cit.*), 200 g. of 8-hydroxyquinoline yielded an equal weight of quinolinic acid, which formed fine needles from acetic acid, m. p. 230° (decomp.); 14 g. of this, through the silver salt, yielded 11 g. of the diethyl ester, b. p. 170°/10 mm. The ester was more conveniently prepared on a larger scale by refluxing the *carefully dried* acid with 10 volumes of absolute alcohol for 6 hours in a current of dry hydrogen chloride. It was isolated in the usual manner, b. p. 175°/15 mm.; yield, 70%.

Ethyl quinolinate (47 g.) was shaken with an excess of aqueous ammonia, saturated at 0°, for 24 hours. Pure quinolinamide (25 g.) separated in white needles, m. p. 209° in agreement with Engler (*Ber.*, 1894, **27**, 1788). The yield was slightly lower if ammonia (*d* 0·880) was used. The methyl ester gave the same result. The corresponding imide was prepared by Sucharda's method (*loc. cit.*) and had m. p. 233° after crystallisation from acetic acid or sublimation.

20 G. of quinolinamide were refluxed for 2 hours with 12 c.c. of acetic anhydride and 11 c.c. of acetic acid. On cooling, the solution deposited 15 g. of 2(or 3)-*cyanopyridine*-3(or 2)-*carboxyamide*, m. p. 255—260° after crystallisation from water (Found: C, 56·9; H, 3·8; N, 28·4. $C_7H_5ON_3$ requires C, 57·2; H, 3·4; N, 28·6%). This substance readily formed blue pigments when heated with metallic reagents. (It is possible that it is actually the cyclic isomeride, iminoquinolinimide.) When the dehydration of the diamide was carried out with acetic anhydride alone, the yield of cyanoamide was lower and the mother-liquors contained a substance, m. p. 150°, with a comparatively low nitrogen content. This was probably the *acetyl* derivative of quinolinimide; the analytical figures indicate that it was not quite pure (Found: C, 56·2; H, 3·2; N, 15·9. $C_9H_6O_3N_2$ requires C, 56·8; H, 3·2; N, 14·7%). It gave no pigments when heated with metallic reagents. A similar product was formed by the action of acetic anhydride on the cyanoamide.

The dinitrile of quinolinic acid could not be obtained by "chemical" dehydration of the diamide or cyanoamide (see below), but was obtained in very poor yield by the following catalytic process suggested by the general method of Reid (*J. Amer. Chem. Soc.*, 1916, **38**, 2128; 1931, **53**, 321). 5 G. of the diamide were placed in one end of a horizontal hard glass tube, the bulk of which was packed with silica gel. The catalyst was heated to 320—350°, and the diamide sublimed in a stream of dry ammonia gas. There was gross decomposition and only 0·4 g. of solid product was isolated, m. p. about 100°, which readily yielded a blue pigment when heated with copper and cuprous chloride. After crystallisation from benzene–light petroleum this melted at 130° and was nearly pure 2 : 3-*dicyanopyridine* (Found: N, 31·5. $C_7H_3N_3$ requires N, 32·6%). When the diamide was heated at 230° with phosphoric oxide, the sublimed product was crude imide, m. p. *ca.* 230° (Found: N, 21·0%). A similar result was obtained by heating the cyanoamide with phosphoric oxide at 270°, the product having m. p. *ca.* 240° (Found: N, 19·8. Calc. for $C_7H_4O_2N_2$: N, 18·9%).

Tetrapyridinoporphyrazines.—A mixture of 5 g. of the cyanoamide and 1 g. of etched magnesium turnings was heated with stirring to 270—280° during 10 minutes. An intense purple reflex rapidly developed. The material was cooled, powdered, stirred with dilute hydrochloric acid to remove free magnesium, washed, and dried. The magnesium compound (4·8 g.) was then dissolved in concentrated sulphuric acid, and the solution poured on ice. The blue precipitate was washed, dried (1·2 g.), and crystallised from chloronaphthalene in an extractor.

Tetra-2 : 3-*pyridinoporphyrazine* (XVII) formed fine blue needles with a purple reflex (0·8 g.) (Found: C, 64·5; H, 2·8; N, 31·6. $C_{28}H_{14}N_{12}$ requires C, 64·8; H, 2·7; N, 32·4%). The rubbing was rather bluer than that of phthalocyanine, and about the same shade as that of cobalt phthalocyanine. The solution in chloronaphthalene was greenish-blue, and in sulphuric acid bright green. The compound was insoluble in alcohol and other low-boiling solvents. Sublimation at low pressures gave a very poor yield of crystalline product. The elimination of metal from the magnesium derivative was improved by using dilute acids. 50 and 75% Sul-

phuric acid (by vol.) gave a 32% recovery of tetrapyridinoporphyrazine. The magnesium pigment was completely dissolved by 10 volumes of 25% sulphuric acid (by vol.), and dilution precipitated tetrapyridinoporphyrazine in 38% yield. No solid salts with sulphuric acid could be isolated. The solubility in relatively dilute acids contrasts with that of phthalocyanine, which only dissolves in sulphuric acid containing about 75% of acid by volume.

1 G. of tetrapyridinoporphyrazine was heated for 4 hours at 160° with 5 c.c. of methyl iodide The solid product (1·2 g.) was rather greener than the parent substance and after extraction with pyridine and alcohol corresponded approximately to a *dimethiodide* (Found: I, 32·7. $C_{28}H_{14}N_{2},2CH_{3}I$ requires I, 31·4%). The iodine was readily removed by boiling aqueous alkali.

A blue copper derivative was prepared both by heating 2 : 3-dicyanopyridine with cuprous chloride at 240° and from quinolinamide, copper and ammonium aminosulphonate at 270°, but it was found impossible to obtain it in a state of analytical purity. In the latter process, 10 g. each of aminosulphonic acid and ammonium carbonate were fused together at 140° until a clear melt was obtained; 2·5 g. of quinolinamide and 0·7 g. of reduced copper were then added, and the temperature raised to 270° until the mass was solid (15 minutes). The product was cooled and extracted successively with boiling water and boiling alcohol, after which a yield of 65% (calc. on the diamide) of a blue powder remained. Purification of this through concentrated sulphuric acid in the usual way was unsatisfactory, as the precipitated material formed a fine suspension which could not be filtered. The copper compound was soluble in 50% sulphuric acid, but use of dilute acids and neutralisation of the suspensions were alike without effect. Crystallisation of the crude pigment from quinoline and chloronaphthalene gave difficulty owing to the low solubility. This necessitated a long period of extraction which led to considerable decomposition. Satisfactory analyses could not therefore be obtained, but from the general behaviour there was no doubt that a considerable proportion of the desired copper derivative was present. The copper compound prepared from the dinitrile gave similar results.

Pyrazine Series.

Diaminomaleinitrile (XIV) * (compare Grischkevitsch-Trochimovski, *loc. cit.*).—After preliminary experiments, consistent yields were obtained as follows: 238 g. of hydrogen cyanide were distilled through a tube of calcium chloride into a strong flask, 1 g. of potassium cyanide was added, and the mixture left corked in the open air for 3—4 days at a mean temperature of 10°. The liquid was then decanted into a fresh vessel, and the process repeated, the last traces of liquid being allowed to evaporate. The rate of polymerisation was at first about 6 g. per day, but later fell to less than half this. The combined yield of solid "azulmin" was 190 g. (80%), which on Soxhlet extraction with ether for 3 days gave 33 g. (17%) of crude tetrameride. If the polymerisation was allowed to proceed without periodic decanting, more of the higher polymerides appeared to be formed. 5 G. of the crude tetrameride on crystallisation from water (charcoal) gave 3·8 g. of diaminomaleinitrile in reddish needles, m. p. 179° (decomp.) (Found: C, 44·3; H, 3·6; N, 50·5. Calc. for $C_{4}H_{4}N_{4}$: C, 44·4; H, 3·7; N, 51·9%). For the following preparations the crude tetrameride could be used.

2 : 3-Dicyanopyrazine (XV), prepared from the tetrameride and glyoxal, following Grischkevitsch-Trochimovski, formed colourless feathery needles from water, m. p. 132° (Found: C, 55·4; H, 1·6; N, 43·2. Calc. for $C_{6}H_{2}N_{4}$: C, 55·4; H, 1·5; N, 43·1%). 1 G. of 2 : 3-dicyanopyrazine was refluxed for 18 hours with 5 c.c. of concentrated hydrochloric acid. The product was evaporated to dryness and extracted with acetone. The extract yielded 0·6 g. of pyrazinemonocarboxylic acid (XVI), which formed needles, m. p. 221° (decomp.), after crystallisation from water (Found: C, 48·7; H, 3·3. Calc. for $C_{5}H_{4}O_{2}N_{2}$: C, 48·4; H, 3·2%). The mother-liquors from this acid yielded a silver salt, from which the same acid was regenerated; there was no sign of the presence of the dicarboxylic acid. 1 G. of 2 : 3-dicyanopyrazine was treated with 10 c.c. of 10% aqueous caustic potash and sufficient alcohol for solution. After 36 hours' refluxing, the alcohol was removed, and the product converted into the silver salt (3 g.), from which 0·8 g. of crude pyrazine-2 : 3-dicarboxylic acid was liberated. As this was difficult to purify by crystallisation, it was decarboxylated by sublimation at 200° into the monocarboxylic acid, m. p. 221° (decomp.) after crystallisation from water. The identity of both these samples of pyrazinemonocarboxylic acid was confirmed by mixed m. p. determinations with authentic material (m. p. 221°, decomp.) prepared from quinoxaline through pyrazinedicarboxylic acid by the method of Gabriel and Sonn (*loc. cit.*).

Substituted Dicyanopyrazines.—A mixture of 0·65 g. of the crude tetrameride, 1 g. of diacetyl,

* The name is used for convenience, although there is evidence that the compound usually reacts as the imino-modification (private communication from Dr. L. E. Hinkel).

0·5 c.c. of glacial acetic, 10 c.c. of water and 10 c.c. of alcohol was heated at 80° for 30 minutes. After the addition of charcoal, the solution was boiled and filtered. The filtrate deposited 2 : 3-*dicyano*-5 : 6-*dimethylpyrazine* in light yellow plates, m. p. 166° (Found : C, 60·7; H, 4·1. $C_8H_6N_4$ requires C, 60·8; H, 3·8%).

To a solution of 0·5 g. of the crude tetrameride, 0·6 c.c. of hydrochloric acid, and 0·5 g. of sodium acetate in 10 c.c. of water on the water-bath, were added 1 g. of benzil and enough alcohol to clear the solution. After 30 minutes' heating, the filtered solution deposited long needles of 2 : 3-*dicyano*-5 : 6-*diphenylpyrazine* (1·5 g.), which formed small plates from alcohol, m. p. 245° (Found : C, 76·3; H, 3·7. $C_{18}H_{10}N_4$ requires C, 76·6; H, 3·6%).

A solution of 1 g. of phenanthraquinone, 0·5 g. of the crystallised tetrameride, and 0·5 c.c. of acetic acid in alcohol was refluxed for 2 hours. 2 : 3-*Dicyanophenanthra*(9′ : 10′ : 5 : 6)*pyrazine* (1 g.) separated partly in the hot, partly on cooling, and crystallised from benzene in golden needles, m. p. 320° (Found : C, 77·5; H, 3·2. $C_{18}H_8N_4$ requires C, 77·1; H, 3·0%).

Tetrapyrazinoporphyrazines.—2 G. of 3 : 4-dicyanopyrazine were heated with 1 g. of cuprous chloride. A blue colour developed at 130°, the internal temperature rose rapidly to *ca.* 250°, and hydrogen chloride was evolved. The powdered product was washed with aqueous ammonia, water, and alcohol, and (2·3 g.) dissolved in concentrated sulphuric acid. The deep blue solution was filtered, and the pigment precipitated with ice in the usual way. Yield, 1·5 g. of *copper tetrapyrazinoporphyrazine tetrahydrate* as a blue solid with a purple lustre. Chlorine and sulphur were absent. After drying in a desiccator over calcium chloride (Found : C, 44·1, 44·2; H, 1·9, 2·3; N, 35·3; Cu, 9·8. $C_{24}H_8N_{16}Cu,4H_2O$ requires C, 43·9; H, 2·4; N, 34·1; Cu, 9·7%), this yielded the stable *trihydrate* after drying in a vacuum over sulphuric acid (Found : C, 45·0; H, 2·3; Cu, 9·8. $C_{24}H_8N_{16}Cu,3H_2O$ requires C, 45·2; H, 2·2; Cu, 10%). The last molecule of water was held very firmly. The tetrahydrate lost 5·67% in weight at 150° (calc. for $2H_2O$, 5·6%), and 8·54% at 200° (calc. for $3H_2O$, 8·46%). The residue then had C, 47·1; H, 1·8; Cu, 11·0%. There was very little loss at 200° in a vacuum and the final product was the *monohydrate* (Found : C, 47·8; H, 1·7; Cu, 10·6. $C_{24}H_8N_{16}Cu,H_2O$ requires C, 47·8; H, 1·7; Cu 10·6%). The monohydrate reverted to the trihydrate in the air of the laboratory (Found : C, 45·7; H, 2·2; N, 35·2; Cu, 10·2%. Calc. for $C_{24}H_8N_{16}Cu,3H_2O$: C, 45·2; H, 2·2; N, 35·2; Cu, 10·0%. Found : gain in weight, 5·1. Calc. for $2H_2O$, 5·6%). The copper analyses enumerated above were calculated from the residue left after combustion. An estimation on the trihydrate by ashing in an open crucible gave a value 10·54% Cu, which was checked by dissolving the ash in nitric acid and estimating the metal volumetrically (Found : Cu, 10·45%). Other preparations of the trihydrate gave products with identical analytical figures.

The trihydrate was practically insoluble in pyridine, quinoline and chloronaphthalene. Attempts to crystallise it by prolonged extraction with quinoline led to decomposition. All forms of copper tetrapyrazinoporphyrazine were blue with a purple reflex, and none could be sublimed. The trihydrate was decolorised on treatment with nitric acid, acid permanganate, or acid ceric sulphate, but only oxalic acid and no pyrazine derivatives could be isolated from the solutions so obtained.

3 : 4-Dicyanopyrazine (4 g.) was heated with excess of etched magnesium at 200° for several hours. The blue solid which slowly formed was washed with dilute acid, water and alcohol and dried in a vacuum over calcium chloride (yield, 2·9 g.) (Found in two different samples : C, 53·4, 54·0; H, 2·3, 2·3; ash 0·6, 1·1. $C_{24}H_{10}N_{16}$ requires C, 55·2; H, 1·9%). The analyses indicated that elimination of the metal was incomplete. The pigment gave a greenish-blue solution in concentrated sulphuric acid, which, on pouring on ice, yielded *tetrapyrazinoporphyrazine tetrahydrate* as a blue powder (Found : C, 48·5; H, 3·0. $C_{24}H_{10}N_{16},4H_2O$ requires C, 48·5; H, 3·0%). Magnesium could not be eliminated completely from the crude magnesium compound by washing with concentrated hydrochloric acid. The pigment, both before and after treatment with sulphuric acid, could not be crystallised from pyridine, quinoline, and chloronaphthalene (in which it was very slightly soluble in the hot); neither could it be sublimed. Similar coloured substances were obtained by heating dicyanopyrazine with calcium ethoxide, stannous chloride, aluminium chloride, reduced copper, cupric chloride, and zinc chloride. The dicyanopyrazines derived from diacetyl, benzil and phenanthraquinone also gave coloured solids with these reagents, which were not examined in detail. The colours changed from blue to green with increasing molecular weight.

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London, S.W. 7.

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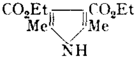
188. *Phthalocyanines. Part X. Experiments in the Pyrrole,* iso*Oxazole, Pyridazine, Furan, and Triazole Series.*

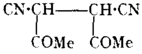
By J. A. BILTON and R. P. LINSTEAD.

THE object of this investigation and the theoretical ideas underlying it are outlined in the preceding paper. Its general result was that no phthalocyanine-like pigment was obtained in any of the five series investigated. In some cases this appears to be a genuine negative and in agreement with theory; in others the result is inconclusive, as suitably close intermediates could not be prepared. In the course of the work a striking difference was observed between the ease with which various heterocyclic *o*-dicarboxylic esters could be converted into the corresponding amides. Amides were readily formed from esters derived from pyridine (preceding paper; Engler, *Ber.*, 1894, **27**, 1788; compare Blumenfeld, *Monatsh.*, 1895, **16**, 700), pyrazine (Gabriel and Sonn, *Ber.*, 1907, **40**, 4850), pyridazine and *iso*oxazole (this paper), but not from the corresponding derivatives of pyrrole, and the conditions necessary for the formation of amides from furan esters are extremely drastic (p. 928). The explanation for this is not apparent.

Derivatives of 2 : 5-Dimethylpyrrole-3 : 4-dicarboxylic Acid.—Attempts to prepare the diamide of this acid from the corresponding readily accessible ethyl ester (I), with the object of dehydrating it to the dinitrile by the usual methods, were frustrated by the remarkable inertia of the ester towards ammonia; the diamide also could not be obtained through the acid chloride. Preparation through the imide was out of the question, as anhydrides of pyrrole-*o*-dicarboxylic acids are difficult to prepare, owing to the ease of decarboxylation, and imides are apparently unknown. The methods successful in the aromatic and in other heterocyclic series (Part IX) were thus useless.

It appeared possible that diacetylsuccinonitrile (II) might be easily prepared from cyanoacetone in the same way as diacetylsuccinic ester from acetoacetic ester. It was then hoped to convert it, by condensation with ammonia in the usual Paal–Knorr manner, into 3 : 4-dicyano-2 : 5-dimethylpyrrole (III).

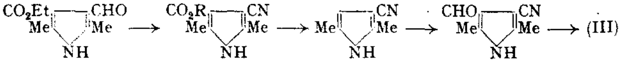

(I.)


(II.)

(III.)

We were unable, however, to prepare (II) by the interaction of the sodio-compound of cyanoacetone with either iodine or *bromocyanoacetone*. Neither could the pyrrole derivative be obtained by direct condensation of cyanoacetone, bromocyanoacetone, and ammonia.

Finally we found that the method used by Fischer and Rothemund (*Ber.*, 1930, **63**, 2255) for the preparation of 3 : 5-dicyano-2 : 4-dimethylpyrrole could be successfully applied to the formation of the isomeric compound (III), in which the cyano-groups are adjacent. The method is outlined in the scheme:

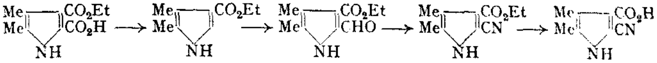

(IV.) (V.) (VI.) (VII.)

Ethyl 3-formyl-2 : 5-dimethylpyrrole-4-carboxylate (IV) and its oxime were prepared from Hantzsch's ethyl 2 : 5-dimethylpyrrole-3-carboxylate by Fischer and Zerweck's method (*Ber.*, 1922, **55**, 1947; 1923, **56**, 524). Dehydration of the oxime yielded ethyl 3-cyano-2 : 5-dimethylpyrrole-4-carboxylate (V, R = Et), which, like the corresponding diester (I), failed to yield an amide when heated under pressure with ammonia. Decarboxylation of the *acid* obtained by hydrolysis (V, R = H) readily yielded *3-cyano-2 : 5-dimethylpyrrole* (VI). This, by the Fischer–Zerweck modification of Gattermann's method, gave *4-formyl-3-cyano-2 : 5-dimethylpyrrole* (VII). The yield of the latter was good and the 3-cyano-group thus has no inhibiting effect on the reaction. It is shown later that a 2-cyano-group, on

the other hand, inhibits the introduction of a 3-formyl group by the same method. The *oxime* of the aldehyde (VII) gave an excellent yield of 3 : *4-dicyano-2 : 5-dimethylpyrrole* (III) on dehydration.

This dinitrile yielded no phthalocyanine-like pigment when treated with metallic reagents under the usual conditions. Its constitution was confirmed by conversion into the cyano-ester (V, R = Et) by alcoholic acid.

Derivatives of 2 : 3-Dimethylpyrrole-4 : 5-dicarboxylic Acid.—For the preparation of the dinitrile of this acid, the most suitable method appeared to be the introduction of a formyl group into 2 : 3-dimethyl-4- or -5-cyanopyrrole, followed by dehydration of the corresponding oxime. The first method attempted is outlined below :



(VIII.) (IX.) (X.) (XI.) (XII.)

Ethyl hydrogen 2 : 3-dimethylpyrrole-4 : 5-dicarboxylate (VIII) (Piloty and Wilke, *Ber.*, 1912, **45**, 2586) was decarboxylated to (IX), and this was converted into the 5-aldehyde (X) and 5-aldoxime (Fischer and Beller, *Annalen*, 1925, **444**, 244). The latter on dehydration yielded the *cyano-ester* (XI) and thence by hydrolysis *5-cyano-2 : 3-dimethylpyrrole-4-carboxylic acid* (XII). At this stage the method broke down unexpectedly, as it was not found possible to decarboxylate (XII) to the corresponding mononitrile (XIII).

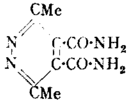
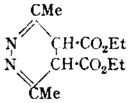
The mononitrile was, however, successfully prepared by converting the acid ester (VIII) into 2 : 3-dimethylpyrrole by Fischer and Nüssler's method (*Annalen*, 1931, **491**, 168), an α-formyl group being introduced in the usual way, and the corresponding oxime (XIV) dehydrated. We were unable to effect the introduction of the β-formyl group by Gattermann's reaction into either the nitrile (XIII), the oxime (XIV), or the corresponding 5-aldehyde.

(XIV.) (XIII.) (XV.) (XVI.)

iso*Oxazole Group.*—The researches of various Italian workers indicated that amides and nitriles of the *iso*oxazole series, unlike their pyrrole analogues, could be prepared by conventional methods (*Gazzetta*, 1915, **45**, i, 362; 1921, **51**, ii, 229; 1929, **59**, 930; 1932, **62**, 436). No diamides or dinitriles were known, but ethyl 5-methyl*iso*oxazole-3 : 4-dicarboxylate, which can be obtained from diacetylsuccinic ester, was a convenient starting material. This ester readily gave the corresponding *diamide* (XV) on treatment with ammonia, and thence by fusion with phosphoric oxide 3 : *4-dicyano-5-methyl*iso*oxazole* (XVI). The structure of this followed from its reconversion into the original diester with alcoholic hydrogen chloride. The dinitrile was hydrolysed by cold aqueous alkali with extraordinary ease into the corresponding *cyanoamide* (either 3 : 4- or 4 : 3-). Quilico and Frori (*Gazzetta*, 1932, **62**, 436) found that 5-cyano*iso*oxazole was readily hydrolysed to the corresponding amide under similar conditions. They also observed that alcoholic alkali led to ring fission with the formation of potassium cyanoacetate. In the present work it was shown that no ring fission had occurred by dehydrating the cyanoamide to the parent dinitrile (XVI). Neither the cyanoamide nor the dinitrile yielded pigments when treated with the usual metallic reagents.

Pyridazine Group.—Here again a convenient starting material in 3 : 6-dimethylpyridazine-4 : 5-dicarboxylic ester could be obtained from diacetylsuccinic ester (Paal and Ubber, *Ber.*, 1903, **36**, 497). This was converted into the *diamide* (XVII) by aqueous ammonia in the cold. The corresponding 4 : 5-dihydro-ester (XVIII), the primary product of the interaction of hydrazine and diacetylsuccinic ester, yielded no diamide under the same conditions. The diamide (XVII) yielded the corresponding *imide* at its melting point and the imide re-formed the diamide with cold aqueous ammonia. This behaviour paralleled that of the

corresponding derivatives of phthalic and quinolinic acids. All attempts to dehydrate the diamide to dinitrile were unsuccessful.

(XVII.)   (XVIII.)

Furan Group.—Reichstein (*Helv. Chim. Acta*, 1930, **13**, 345; 1931, **14**, 1277) has observed that the Gattermann aldehyde synthesis can only be applied to the α-positions of the furan ring. Hence the synthesis of dinitriles through aldoximes appeared difficult. Seka has found (*Ber.*, 1924, **57**, 1864) that 2 : 5-dimethylfuran-3 : 4-dicarboxylic ester only yields the corresponding diamide with great difficulty. We can confirm this; the yields obtained in our experiments were so small that dehydration of the diamide could not be investigated. This resistance to amide formation appears to be a general property of furan esters, for another promising line of attack was held up by the fact that the *methyl* ester of 5-cyano-3-methylfuran-4-carboxylic acid (Rinkes, *Rec. trav. chim.*, 1931, **50**, 1127) failed to yield a cyanoamide on treatment with aqueous or alcoholic ammonia.

Triazole Group.—Grischkevitsch-Trochimovski (*Rocz. Chem.*, 1921, **1**, 468) and Fialkov (*Bull. Soc. chim.*, 1927, **41**, 1209) have shown that the tetra-amide of hydrogen cyanide, reacting as diaminomaleinitrile (XIX), yields dicyanotriazole (XX) on treatment with nitrous acid.

(XIX.) (XX.)

This substance failed to yield pigments of the phthalocyanine type when heated with metallic reagents. This was not surprising, as it is among the strongest of organic acids (Fialkov, *loc. cit.*). The *N*-methyl ether also yielded no pigments, possibly owing to the difficulty of forming an ortho-ring.

Grischkevitsch-Trochimovski (*loc. cit.*; *J. Russ. Phys. Chem. Soc.*, 1924, **55**, 548) states that dicyanotriazole is first formed in a yellow modification, which yields a colourless form on sublimation. Our yellow reaction product yielded a practically colourless dinitrile on crystallisation and it appears probable that the original colour is due to the presence of a trace of impurity. The evidence adduced by Grischkevitsch-Trochimovski and by Fialkov (*locc. cit.*) for the existence of two distinct forms of the dinitrile is very slight.

Experimental.

3 : 4-*Dicyanopyrrole Series*.

Method 1.—*Diacetylsuccinic ester*. In the routine preparation of this ester by Knorr's reaction (*Ber.*, 1894, **27**, 1155) "molecular" sodium was found preferable to sodium wire. 260 G. of ethyl acetoacetate were gradually added to 48 g. of "molecular" sodium under 3 l. of anhydrous ether, the mixture being shaken and cooled in ice when necessary. The nearly solid paste was treated with shaking with 210 g. of iodine dissolved in dry ether. After an hour's standing, the ethereal solution was filtered and evaporated. Diacetylsuccinic ester, which crystallised from the residue, was pressed on a tile and crystallised from 50% acetic acid. Yield, 119 g. (46%); m. p. 82—85°, raised to 88° by recrystallisation. In larger batches it was found advisable to add solid iodine with only enough ether to keep the mixture mobile. When sodium wire was used, the above quantities give 100 g. of ester, in agreement with Knorr.

2 : 5-Dimethylpyrrole-3 : 4-dicarboxylic ester (I), m. p. 91°, was prepared from this in quantitative yield by treatment with aqueous ammonia (*d* 0·880) or, better, with a solution of ammonium acetate in acetic acid (Knorr, *Ber.*, 1885, **18**, 299). Hydrolysis of the ester was troublesome; the following procedure, modified from that of Knorr (*ibid.*, p. 1561), was used: A solution of 20 g. of the ester in the minimum amount of hot alcohol was treated with 100 c.c. of 12% aqueous caustic potash and enough alcohol to effect solution. The alcohol was boiled off

during 2 hours, and the solution cooled in ice and acidified with mineral acid. The mixture of diacid and acid ester was taken up in the minimum quantity of caustic soda solution, and the acid ester precipitated by adding acetic acid to the ice-cold solution until it was acid to litmus. The diacid was then precipitated from the ice-cold filtrate by the addition of dilute sulphuric acid until it was acid to Congo-red. The diacid formed needles from dilute alcohol, m. p. 250°; yield, 20%. No diamide could be obtained by treating the diacid successively with thionyl chloride or phosphorus pentachloride and ammonia under a variety of conditions.

2 : 5-Dimethylpyrrole-3 : 4-dicarboxylic ester was unchanged after being heated at 100° for 2 days with aqueous ammonia (*d* 0·880), or after 3½ days' treatment under pressure at 100° with methyl-alcoholic ammonia, saturated at 0°.

Methyl acetoacetate (Komnenos, *Monatsh.*, 1910, **31**, 687) was converted into *methyl* 1 : 2-*diacetylsuccinate* by the method described above for the ethyl ester. The methyl ester only solidified after distillation, b. p. 120°/20 mm., and separated from dilute alcohol in small white crystals, m. p. 113·5° (Found : C, 52·3; H, 6·0. $C_{10}H_{14}O_6$ requires C, 52·2; H, 6·2%). Treatment of this ester with aqueous ammonia yielded only a brown oil and the reaction was not further investigated.

Method 2.—Cyanoacetone (Holtzwart, *J. pr. Chem.*, 1889, **39**, 238) was prepared from β-iminobutyronitrile (Moir, J., 1902, **81**, 101) immediately before use and was kept in ethereal solution, as evaporation led to the formation of a substance, m. p. 265°, apparently the dimeride (compare Moir, *loc. cit.*). The ethereal solution from 2 g. of iminobutyronitrile was treated with an excess of sodium in flat, freshly cut plates. The white sodio-compound was filtered off and separated mechanically from the excess of sodium; yield, 26%. When it was treated with phenylhydrazine in dilute acetic acid solution, it yielded the hydrazone, m. p. 96°, reported by Holtzwart (*loc. cit.*). When an ethereal suspension of the sodio-compound was left overnight with iodine, dissolved in ether, no reaction occurred.

The ethereal solution of cyanoacetone from 2 g. of iminobutyronitrile was treated with 4 g. of bromine (1 mol.) and kept overnight. A yellow oil separated, which was distilled after removal of solvent. *α-Bromocyanoacetone* boiled at 43°/12 mm. (Found : Br, 51·7, 50·1. C_4H_4ONBr requires Br, 49·4%); a fraction, b. p. 99°/12 mm., was also obtained. Bromocyanoacetone was soluble in light petroleum and was precipitated from such solutions by the addition of ether. On standing, it decomposed with the formation of ammonium bromide. An attempt to condense cyanoacetone with bromocyanoacetone and aqueous ammonia directly to a pyrrole derivative was fruitless. Attempted condensation of the sodio- and the bromo-derivative of cyanoacetone to diacetylsuccinonitrile was also unsuccessful.

Method 3.—Ethyl 2 : 5-dimethylpyrrole-3-carboxylate was prepared in consistent yields of 43% by Hantzsch's reaction (*Ber.*, 1890, **23**, 1474), and converted successively into the 4-formyl derivative (IV) (yield 77%, m. p. 151°), and the 4-aldoxime (theoretical yield, m. p. 223°) by the methods of Fischer and Zerweck (*locc. cit.*). The aldoxime was dehydrated by ½ hour's boiling with acetic anhydride and dry sodium acetate (Fischer and Zerweck, *loc. cit.*, 1923). The product was added to hot water, the solution evaporated nearly to dryness and diluted with hot water, and the separated ethyl 4-cyano-2 : 5-dimethylpyrrole-3-carboxylate (V, R = Et) crystallised from water to a m. p. of 152°. For large batches it was convenient to reduce the proportion of anhydride from that used by the previous workers, although the yield was slightly depressed. Thus, 85 g. of oxime, 85 g. of sodium acetate, and 800 g. of acetic anhydride gave 61 g. of the cyano-ester (78%). This cyano-ester was not converted into the corresponding cyano-amide on treatment at room temperature with aqueous ammonia, saturated at 0°, or by heating in an autoclave with methyl-alcoholic ammonia (saturated at − 20°) for 6 hours at 135° and 200 lb./sq. in. pressure. It was recovered unchanged from both experiments, m. p. and mixed m. p. 152°.

10 G. of the cyano-ester were heated to boiling with 100 c.c. of 25% aqueous caustic soda and just sufficient ethyl alcohol to effect solution. The solution was boiled for 30 minutes, water being added from time to time to dissolve the precipitate; alcohol was removed, and the product acidified at 0° with dilute hydrochloric acid. The flocculent precipitate of *3-cyano-2 : 5-dimethylpyrrole-4-carboxylic acid* (V, R = H) was crystallised from water. Yield, theoretical; m. p. 288° (decomp.) (Found : C, 58·4; H, 5·0. $C_8H_8O_2N_2$ requires C, 58·5; H, 4·9%). The sodium salt appeared to be rather sparingly soluble in water. 26 G. of this acid were decarboxylated in an oil-bath at 200°/13 mm., *3-cyano-2 : 5-dimethylpyrrole* (VI) distilling as a brownish-red product, which crystallised from water (charcoal) in white needles, m. p. 89°; yield, 73% (Found : N, 23·5. $C_7H_8N_2$ requires N, 23·3%).

A solution of 13·1 g. of 3-cyano-2 : 5-dimethylpyrrole in 45 c.c. of dry chloroform and 45 c.c.

of dry ether was treated with 40 c.c. of dry ice-cold liquid hydrogen cyanide, and a current of dry hydrogen chloride was passed through the solution at 0°. The red imine hydrochloride soon separated from the green-fluorescing solution. After an hour's passage of the gas, the product was left overnight at 0°, and the precipitate collected and washed with dry ether. The imine hydrochloride was decomposed first with ice-water and finally by warming on the water-bath. The yellow flocculent precipitate of *4-formyl-3-cyano-2 : 5-dimethylpyrrole* (VII) was filtered off, *washed with water, and crystallised from 50% alcohol, forming yellow needles, m. p. 207°; yield, 81% (Found: C, 64·8; H, 5·5. $C_8H_8ON_2$ requires C, 64·9; H, 5·4%).* 10 G. of this aldehyde were dissolved in warm alcohol, and water added to give a faint turbidity. A concentrated aqueous solution of 10 g. of hydroxylamine hydrochloride, neutralised with caustic soda, was added and the mixture heated gently on a water-bath. After 15 minutes, the solution was cooled, and the *oxime* collected; it crystallised from dilute alcohol in long white needles, which softened at 214°, turned brown at 220°, and melted at 223°; yield, theoretical (Found: N, 26·0. $C_8H_9ON_3$ requires N, 25·8%).

10 G. of this aldoxime were refluxed for ½ hour with 500 c.c. of acetic anhydride and 10 g. of sodium acetate, and the product worked up as in the previous similar dehydration. 3 : 4-*Dicyano-2 : 5-dimethylpyrrole* (III) formed white needles from dilute alcohol, m. p. 239° (brown at 200°); yield, 89% (Found: C, 65·9; H, 4·9; N, 29·2. $C_8H_7N_3$ requires C, 66·2; H, 4·8; N, 29·0%).

Dry hydrogen chloride was passed through a solution of 3 g. of the dinitrile in 100 c.c. of absolute alcohol for 8 hours at room temperature. The solution soon turned deep red and deposited a white precipitate. Filtration and evaporation of the alcohol then yielded long white needles of ethyl 4-cyano-2 : 5-dimethylpyrrole-3-carboxylate, m. p. and mixed m. p. 148°. This was further identified by conversion successively into 4-cyano-2 : 5-dimethylpyrrole-3-carboxylic acid, m. p. and mixed m. p. 286°, and 4-cyano-2 : 5-dimethylpyrrole, m. p. and mixed m. p. 89°.

3 : 4-Dicyano-2 : 5-dimethylpyrrole was heated with the following reagents from 200° to 280° during 1 hour: Sodium amyloxide, stannous chloride, copper-bronze, cuprous chloride, zinc and magnesium. In each case there was charring and no sign of the formation of a pigment of the phthalocyanine type. Negative results were also obtained by heating the dinitrile at 200° for 7 hours with the following: β-naphthol, acetamide, glycerol, copper-bronze, etched magnesium, calcium oxide.

2 : 3-Dicyanopyrrole Series.

Methyl α-isoNitrosoethyl Ketone (cf. Diels and Jost, *Ber.*, 1932, **65**, 3292).—A mixture of 834 g. of methyl ethyl ketone and 28 c.c. of concentrated hydrochloric acid was treated during 2½ hours with 1333 g. of amyl nitrite, the temperature being kept at 50—60°. The product was treated with 1 kg. of powdered ice and 1008 g. of 33% caustic soda solution and stirred for 2 hours, and the *iso*nitroso-compound isolated following the directions of Fischer and Orth (" Die Chemie des Pyrrols," p. 408). Yield, 680 g.; thorough extraction with ether was essential.

The *iso*nitroso-compound was reduced on a large scale as follows (cf. Diels and Jost, *loc. cit.*; Künne, *Ber.*, 1895, **28**, 2036). 300 G. of methyl *iso*nitrosoethyl ketone were added slowly to a rapidly stirred solution of 1985 g. of stannous chloride dihydrate in 1666 c.c. of concentrated hydrochloric acid, the reaction being controlled by cooling in ice-water. The cold solution was diluted with 12 l. of water, hydrogen sulphide passed in, tin sulphide allowed to settle, and the liquid filtered. The treatment with hydrogen sulphide was repeated to ensure complete removal of the tin. The final filtrate was evaporated to 2 l., and the removal of water completed under reduced pressure at 50—60°. The residual black oil was dissolved at 30° in 22 parts of absolute alcohol, the ammonium chloride filtered off, and dry ether added until the turbidity produced just dissolved on shaking. On standing overnight at 0° in a closed vessel, fine white crystals of aminobutanone hydrochloride (135 g., 37%) separated, which were filtered off and washed with an anhydrous mixture of alcohol and ether. This process, although tedious, was found more convenient than that involving electrolytic removal of the tin (Fischer and Orth, *op. cit.*, p. 410).

Ethyl hydrogen 2 : 3-dimethylpyrrole-4 : 5-dicarboxylate (VIII), m. p. 201°, was prepared in 26% yield by condensing this hydrochloride with oxalacetic ester in aqueous alkali (Piloty and Wilke, *loc. cit.*; *Ber.*, 1913, **46**, 1597; Fischer and Kutscher, *Annalen*, 1930, **481**, 199).

Attempted Preparations of 4 : 5-Dicyano-2 : 3-dimethylpyrrole.—(1) Via *5-cyano-2 : 3-dimethylpyrrole-4-carboxylic acid.* Ethyl hydrogen 2 : 3-dimethylpyrrole-4 : 5-dicarboxylate was decarboxylated to ethyl 2 : 3-dimethylpyrrole-4-carboxylate (IX) at 225° in a stream of

carbon dioxide. Yield, nearly theoretical; m. p. 110° (cf. Piloty and Wilke, *Ber.*, 1912, **45**, 2588). The 5-formyl group was introduced and the corresponding aldoxime prepared following Fischer and Beller (*loc. cit.*).

3 G. of 4-carbethoxy-2 : 3-dimethylpyrrole-5-aldoxime were refluxed for ½ hour with 150 c.c. of acetic anhydride and 3 g. of sodium acetate. *Ethyl 5-cyano-2 : 3-dimethylpyrrole-4-carboxylate* (XI) was isolated in fine powdery crystals, m. p. 180°, from the product by the usual procedure; yield, 81% (Found : C, 62·4; H, 6·1. $C_{10}H_{12}O_2N_2$ requires C, 62·5; H, 6·3%). 3·7 G. of this cyano-ester were hydrolysed by 1 hour's boiling with 44 c.c. of 25% aqueous caustic potash and sufficient alcohol for solution. After removal of the alcohol, *5-cyano-2 : 3-dimethylpyrrole-4-carboxylic acid* (XII) was precipitated by the addition of mineral acid; it crystallised from 50% alcohol (charcoal) in stout shining crystals, m. p. 242°, decomp. 250°; yield, 94% (Found : C, 58·3; H, 4·8. $C_8H_8O_2N_2$ requires C, 58·5; H, 4·9%). This cyano-acid was very stable. No carbon dioxide was evolved when it was liberated from aqueous solutions of its salts at room temperature. Heated at 4 mm., it charred without decarboxylation. Heated in glycerol at 280° for 30 minutes, it yielded an unidentified solid, m. p. 176°, which was not the corresponding cyanodimethylpyrrole (m. p. 121·5°). It yielded no phthalocyanine-like pigment when heated with copper and ammonium aminosulphonate.

(2) Via *2 : 3-dimethylpyrrole*. 2 : 3-Dimethylpyrrole was prepared from ethyl hydrogen 2 : 3-dimethylpyrrole-4 : 5-dicarboxylate following Fischer and Nüssler (*loc. cit.*). The 5-formyl group was introduced (Fischer and Orth, *op. cit.*, p. 154) and thence the 5-aldoxime (XIV), m. p. 121°, was prepared. 1 G. of this oxime was dehydrated in the usual way with an equal weight of sodium acetate in 50 c.c. of acetic anhydride to *5-cyano-2 : 3-dimethylpyrrole* (XIII), which formed long glistening needles from water (charcoal), m. p. 121·5°; yield, 66% (Found : C, 70·3; H, 6·7; N, 23·2. $C_7H_8N_2$ requires C, 70·0; H, 6·7; N, 23·3%). This failed to react with hydrogen cyanide and hydrogen chloride under the usual conditions either in a mixture of ether and chloroform at 0° or in chloroform alone at room temperature. The corresponding 5-aldoxime and 5-aldehyde also failed to react under these conditions.

iso*Oxazole Series.*

5 G. of ethyl 5-methyl*iso*oxazole-3 : 4-dicarboxylate, m. p. 56° (Schmidt and Widman, *Ber.*, 1908, **41**, 1252), were shaken for several hours in a closed flask with an excess of aqueous ammonia (*d* 0·880). The long white needles of *5-methyl*iso*oxazole-3 : 4-dicarboxyamide* (XV) were filtered off, washed with water, and crystallised from alcohol. Yield, 67%; m. p. 216° after softening at 195° (Found : N, 25·1. $C_6H_7O_3N_3$ requires N, 24·9%). Under 5 mm., the diamide sublimed unchanged.

A mixture of 2 g. of the diamide and 4 g. of phosphoric oxide were heated by means of a glycerol bath in a vertical tube with a wide horizontal side arm. At about 115°/5 mm. in a slow stream of dry air a colourless liquid distilled into the side arm and solidified. At 175° a solid sublimed, and condensed much nearer the vertical tube than the first distillate, which it did not contaminate. The sublimate was the diamide, m. p. and mixed m. p. 216°. The liquid was *3 : 4-dicyano-5-methyl*iso*oxazole* (XVI), which formed a mass of radiating needles, m. p. 32°, b. p. 115°/12 mm. without decomposition and 245°/760 mm. with some decomposition; yield, 1·1 g. (70%) (Found : C, 54·1; H, 2·3; N, 32·1. $C_6H_3ON_3$ requires C, 54·1; H, 2·3; N, 31·6%). About 3 hours' heating at 115—120°/5 mm. were necessary for the preparation of the dinitrile in a state of purity. At 160°/5 mm., the diamide and phosphoric oxide yielded a distillate in 30 minutes, but the product would not solidify. The diamide was unchanged by 6 hours' refluxing with an excess of acetic anhydride.

A current of dry hydrogen chloride was passed through a solution of 1 g. of 3 : 4-dicyano-5-methyl*iso*oxazole in absolute alcohol for 1½ hours, after which no further precipitation occurred. The precipitate was retained (A); the filtrate was freed from alcohol and poured on ice. Ethyl 5-methyl*iso*oxazole-3 : 4-dicarboxylate was precipitated; it was identified by m. p. and mixed m. p. (55°) and by conversion into the diamide, m. p. 216°. The precipitate (A) was washed free from ammonium chloride with water and crystallised from water or alcohol. White plates of 4(or 3)*-cyano-5-methyl*iso*oxazole-*3(or 4)*-carboxyamide* separated, m. p. 225°, depressed to 191° on admixture with the diamide (Found : C, 48·1; H, 3·4. $C_6H_5O_2N_3$ requires C, 47·7; H, 3·3%). This cyanoamide was also readily formed by shaking the dinitrile for a few minutes with 10% aqueous caustic potash; it was identified by m. p. and mixed m. p. (225°) and by analysis (Found : C, 47·4; H, 3·4%).

3 : 4-Dicyano-5-methyl*iso*oxazole yielded no pigment when heated under the usual conditions

with copper-bronze, cuprous chloride, aluminium chloride, etched magnesium, zinc or sodium amyloxide.

Pyridazine Series.

Ethyl 3 : 6-dimethyl-4 : 5-dihydropyridazine-4 : 5-dicarboxylate (XVIII) was prepared from diacetylsuccinic ester in 91% yield by the method of Paal and Ubber (*loc. cit.*). There was no indication of the formation of a diamide when it was shaken for some time with concentrated aqueous ammonia. It was oxidised to ethyl 3 : 6-dimethylpyridazine-4 : 5-dicarboxylate following Paal and Ubber (*loc. cit.*). 25 G. of the latter were shaken vigorously with an excess of aqueous ammonia (*d* 0·880) and kept overnight. 3 : 6-*Dimethylpyridazine*-4 : 5-*dicarboxyamide* (XVII) separated as a white powder, which was washed thoroughly with cold water, hot alcohol and ether. Yield, theoretical; m. p. 240°, not very sharp owing to charring and sublimation of the corresponding imide (Found: C, 49·1; H, 5·4; N, 28·4. $C_8H_{10}O_2N_4$ requires C, 49·5; H, 5·2; N, 28·9%). The diamide was insoluble in ether, alcohol, water, pyridine and hydrocarbons. It was hydrolysed slowly by cold aqueous caustic soda and decomposed by hot water. It was also readily prepared by passing dry ammonia gas through an alcoholic solution of the diester at room temperature.

The diamide at 240°/10 mm. gave a sublimate of long yellowish needles of the corresponding imide. There was some gross decomposition, which also occurred when the imide was resublimed. 3 : 6-*Dimethylpyridazine*-4 : 5-*dicarboxyimide* formed needles from alcohol, m. p. 240° (decomp.); yield, 44% (Found: C, 54·3; H, 3·7; N, 23·9. $C_8H_7O_2N_3$ requires C, 54·2; H, 3·95; N, 23·7%). The imide re-formed the diamide when ammonia was passed through its alcoholic solution.

Unsuccessful attempts were made to prepare a copper pigment of the phthalocyanine type direct from the imide by (i) the action of reduced copper and ammonium aminosulphonate at 200—240° and (ii) the action of cupric chloride and urea at 210°.

The following attempts were made to prepare the dinitrile or the cyanoamide from the diamide: (i) phosphoric oxide at 180—240°/2 mm. yielded a little imide and produced much decomposition; (ii) carbonyl chloride at 60° (passed into a pyridine solution) yielded unchanged diamide and a water-soluble oil; (iii) acetic anhydride at various temperatures from 20° to the b. p. also gave unchanged diamide, imide, and water-soluble material.

The action of thionyl chloride or phosphorus pentachloride on 3 : 6-dimethylpyridazine-4 : 5-dicarboxylic acid (Paal and Ubber, *loc. cit.*) yielded no acid chloride, apparently owing to ring fission.

Furan Series.

Ethyl 2 : 5-dimethylfuran-3 : 4-dicarboxylate was prepared from diacetylsuccinic ester in 94% yield by Knorr's method (*Ber.*, 1884, **17**, 2863). The conversion into the corresponding diamide (compare Seka, *loc. cit.*) was very difficult. For instance, 17 g. of the ester were heated at 90° and 700 lb./sq. in. for 24 hours with a large excess of liquid ammonia, 1 g. of diamide being formed and 15 g. of unchanged ester being recovered. The diamide after several crystallisations from water melted at 236° (sealed tube). Seka gives m. p. 243—244°.

The diamide (500 mg.) was refluxed for 6 hours with acetic anhydride (3 c.c.), and the hot solution added to water. White bunches of needles of 4-*cyano*-2 : 5-*dimethylfuran*-3-*carboxylic acid* separated on cooling, and were recrystallised from water (charcoal); m. p. 174° (Found: C, 58·6; H, 4·6. $C_8H_7O_3N$ requires C, 58·2; H, 4·2%). The acid was soluble with effervescence in aqueous sodium bicarbonate, and was therefore not the corresponding 3 : 4-dicarboxyimide.

11·7 G. of 5-cyano-3-methylfuran-4-carboxylic acid, m. p. 204° (Rinkes, *loc. cit.*), were converted into the silver salt, which was refluxed for 3 days with 9·5 c.c. of methyl iodide in 200 c.c. of dry ether. Removal of the solvent then left an oil, which solidified on cooling and was extracted with benzene. The benzene was removed, and the residual *methyl* ester crystallised from water (charcoal), giving stout needles, m. p. 49°; yield, 26% (Found: C, 58·3; H, 4·4. $C_8H_7O_3N$ requires C, 58·2; H, 4·2%). This ester was hydrolysed when kept with aqueous ammonia (*d* 0·880) overnight, and remained unchanged after being kept in alcoholic ammonia at 50° for 2 days.

Triazole Series (With J. M. Wright).

Diaminomaleinitrile (XIX) (Linstead, Noble, and Wright, preceding paper) was converted into dicyanotriazole (XX), following Grischkevitsch-Trochimovski and Fialkov (*locc. cit.*). The yellow crystalline product was recrystallised from ether–light petroleum, which yielded clear, practically colourless prisms, m. p. 145—148° (lit., 145—150°[5]). The dinitrile is immediately soluble with effervescence in aqueous sodium bicarbonate, and a dilute aqueous solution dissolves

zinc with evolution of hydrogen. The silver salt is precipitated by the addition of silver nitrate and is not dissolved by the cautious addition of dilute nitric acid. Warming with an excess of nitric acid converts the flocculent silver salt into a microcrystalline precipitate of the free dicyanotriazole. The dinitrile does not form a methyl ether when boiled with methanol alone.

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189. *Phthalocyanines. Part XI. The Preparation of Octaphenylporphyrazines from Diphenylmaleinitrile.*

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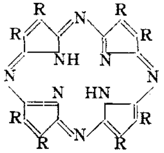
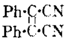
We have been engaged for some years in these laboratories on attempts to synthesise compounds containing the simple porphyrazine system (I). The general method of attack has been to treat the nitrogenous derivatives of acids of the maleic series with metallic reagents, under conditions which result in the formation of phthalocyanines from the corresponding derivatives of phthalic acid. Experiments on various maleic acids of the aliphatic and alicyclic series are still in progress; in the present paper we describe the first successful syntheses.

(I.)* 


(II.)

(III.)

Diphenylmaleinitrile (II) is especially suitable for the preparation of porphyrazines because it is comparatively easily obtained, is stable in the *cis*-form, and has a high thermal stability (even at 300° there is no detectable conversion into the *trans*-form). The *cis*-configuration follows from the ease of conversion into the imide (III) or, *via* the acid, into the corresponding anhydride.

When the nitrile is heated with metallic derivatives such as cuprous chloride, stannous chloride, or litharge at about 250° or with metallic magnesium or copper at 270—275°, vigorous exothermic reactions occur with the production in excellent yield of intensely green metallic octaphenylporphyrazines. The reactions are parallel to those of phthalonitrile (Dent and Linstead, J., 1934, 1027; Barrett, Dent, and Linstead, J., 1936, 1719), but a higher temperature is required for their inception. The reaction with the bivalent metals is the simple one: $4C_{16}H_{10}N_2 + \text{Met.} \longrightarrow (C_{16}H_{10}N_2)_4\text{Met.}$ Cuprous chloride gives a monochlorinated porphyrazine by the reaction $4C_{16}H_{10}N_2 + Cu_2Cl_2 \longrightarrow (C_{16}H_{10}N_2)_3Cu(C_{16}H_9N_2Cl) + Cu + HCl$ even when it is used in excess. Phthalonitrile gives an almost entirely *unchlorinated* pigment under these conditions, and nuclear chlorination appears to be more easily effected in the present series.

The parent octaphenylporphyrazine could not be easily prepared through the sodium compound, as in the phthalocyanine series (Linstead and Lowe, J., 1934, 1022), for example, by heating the nitrile with sodium amyloxide, owing to the facility of hydrolysis to diphenylmaleinimide (III). On the other hand, the series resembles the phthalocyanine and porphyrin in that the metal is eliminated by the action of suitable acids on the *magnesium* derivative to yield the parent *octaphenylporphyrazine* (I, R = Ph). This reaction is not

* In the metallic derivatives a bivalent metal, as usual, takes the place of the two imino-hydrogen atoms inside the great ring.

always straightforward. The use of sulphuric acid leads to sulphonation of the phenyl groups, and the best results are obtained with boiling dilute hydrochloric acid. Formic acid has a considerable solvent action, the metal is quickly removed, and the free porphyrazine is isolated as a *diformate*, which yields the parent compound on treatment with alkali. If acetic or oxalic acid is used in place of formic acid, magnesium octaphenylporphyrazine yields a salt without elimination of the metal. This property of forming a salt with an organic acid has not been so far observed in the phthalocyanine group, although zinc phthalocyanine yields a hydrochloride (Barrett, Dent, and Linstead, *loc. cit.*). We do not know which of the two types of nitrogen atom is concerned in these salt formations.

Octaphenylporphyrazine and its metallic derivatives are purplish-black microcrystalline solids, yielding green amorphous powders. Of the compounds studied, the tin derivative was the dullest, the metal-free and the copper compound intermediate, and the magnesium derivative the brightest green. Unlike the corresponding phthalocyanines, these substances are appreciably soluble in cold organic solvents, such as benzene and acetone, forming emerald-green solutions. They could not be obtained in a macrocrystalline form from these solutions, or by sublimation, and were best purified by chromatographic adsorption on alumina from a benzene solution, followed by elution with pyridine. The various members of the group were not adsorbed equally easily and the magnesium and the copper derivative could be sharply separated in this way. The porphyrazines appear to be the first complex synthetic pigments to have been purified by this method. It is not applicable to phthalocyanines owing to their insolubility.

These compounds are given the porphyrazine structure, analogous to that now definitely established for phthalocyanine, for the following reasons: (i) The method of preparation is exactly analogous to that of phthalocyanines and proceeds smoothly without side reaction. (ii) Analyses correspond to the type $(C_{16}H_{10}N_2)_4H_2$ or $(C_{16}H_{10}N_2)_4Met^{II}$. (iii) Cryoscopic determinations of molecular weights (in camphor) support this formula. These were not possible in the phthalocyanine group, for which molecular weights were obtained with great difficulty in one case ebullioscopically (Linstead and Lowe, J., 1934, **1031**) and, more generally, from a combination of *X*-ray measurements and elementary analysis of the metallic derivatives (Robertson, Linstead, and Dent, *Nature*, 1935, **134**, 506). (iv) There is a general resemblance in chemical properties, in the resistance to heat, alkalis, and, to some extent, acids. The metallic derivatives are comparable in stability.

A distinctive property of the octaphenylporphyrazines is their resistance towards oxidation by acid ceric sulphate, which oxidises phthalocyanines smoothly to phthalimide. The magnesium derivative, however, rapidly reduced potassium permanganate in warm acetone. Derivatives of diphenylmaleic acid could not be isolated, the oxidation product being benzoic acid. This reaction serves to show that there has been no interaction between the phenyl groups, for example, with the formation of a phenanthrene arrangement.

Solutions of magnesium octaphenylporphyrazine, but apparently not those of the copper derivative, show a beautiful rose-red fluorescence in ultra-violet light. This is paralleled in the phthalocyanine and the porphyrin group and will form the subject of a future communication.

Treatment of *p*-nitrophenylacetonitrile with sodium methoxide and iodine yielded *di*-p-*nitrophenylmaleinitrile*. This condensed with copper and with magnesium at about 300° to yield octa(nitrophenyl)porphyrazines, almost indistinguishable from the corresponding un-nitrated compounds, except that solutions of the magnesium derivative of the nitrophenylporphyrazine do not fluoresce. This is a normal result of the introduction of a nitro-group. The derived di-*p*-aminophenylmaleinitrile did not appear to yield similar pigments.

EXPERIMENTAL.

Analytical Notes.—Consistent values for the carbon and hydrogen content of octaphenylporphyrazine derivatives were obtained when the substance in the combustion boat was covered with a layer of potassium dichromate. Without this, the results were low and irregular. In macro-Dumas determinations of nitrogen, combustion had to be very prolonged to give satisfactory results; normal micro-Dumas estimations were always low. All the porphyrazine derivatives described were dried at 100° for at least 3 hours.

Diphenylmaleinitrile (II).—The method of Chalenay and Knoevenagel (*Ber.*, 1892, **25**, 288; cf. Ramart-Lucas and Hoch, *Ann. Chim.*, 1930, **13**, 385) was improved as follows: A cold solution of sodium (18·4 g.) in methanol (300 c.c.) was dropped during 30 minutes into an ice-cooled, stirred mixture of iodine (101·6 g.), phenylacetonitrile (46·8 g.), and ether (1500 c.c.). The product was washed successively with water, dilute sodium thiosulphate solution and water and dried over sodium sulphate. Removal of the solvent left an impure orange-coloured, often lachrymatory, solid. Direct crystallisation was tedious and wasteful. Rapid vacuum distillation yielded phenylacetonitrile (3 g.), a lachrymatory fraction boiling up to 150°/18 mm., probably mainly iodophenylacetonitrile (9 g.), and 20—22 g. (50%) of diphenylmaleinitrile, b. p. 230—235°/18 mm., which solidified to a faintly yellow, crystalline mass. This melted at 156—158° and was sufficiently pure for preparative purposes. Crystallisation from benzene gave pure white needles, m. p. 158°. The crude orange dinitrile could also be purified by adsorption of the impurities on alumina from a benzene solution.

Diphenylmaleinitrile exhibits some remarkable colour reactions apparently not directly related to the formation of porphyrazines described later; *e.g.*, cold sodium ethoxide in alcohol or benzene produces an intense green colour which fades after some 20 minutes to a yellow. The yellow solution in benzene becomes on acidification a magnificent blue with a red fluorescence, but this colour also fades in a few hours. The only solids isolable from these solutions were diphenylmaleinimide (III) and unchanged dinitrile. After 20 minutes at 80° mixtures of the nitrile with sodium alkoxides had become intensely green and yielded the imide contaminated with a little octaphenylporphyrazine. The yield of pigment by this process was very poor. The imide produced in these experiments was identified by m. p. 213°, alone and admixed with material prepared by the method of Reimer (*Ber.*, 1881, **14**, 1800), and by analysis (Found: C, 76·4; H, 4·6. Calc.: C, 77·1; H, 4·4%).

Magnesium and Metal-free Octaphenylporphyrazines.—A mixture of 5 g. of the nitrile and 0·5 g. of magnesium powder was heated to 275° (salt-bath temperature). The melt became intensely green and after 10 minutes had set to a crystalline mass with a fine purple sheen. The product was ground, freed from excess of metal with 25% acetic acid, and then digested with hot 10% caustic soda solution to break down the acetate of the complex (see below) and to hydrolyse unchanged nitrile. The resulting *magnesium octaphenylporphyrazine* was washed thoroughly with hot water and dried. Yield, 4·8 g. (92%) of a purplish-black powder (Found: C, 81·5; H, 4·3; N, 11·75; Mg, 2·5. $C_{64}H_{40}N_8Mg$ requires C, 81·35; H, 4·2; N, 11·9; Mg, 2·6%). The magnesium was determined as MgO after oxidation with nitric acid and ignition.

A solution of 0·6 g. of the compound in 300 c.c. of benzene was run through a 20 × 1·5 cm. column of Merck alumina (*nach Brockmann*). The chromatograph was obtained as a broad green band separating minute quantities of brown impurities. The green zone was eluted with pyridine, the solution concentrated under reduced pressure to 30 c.c. and poured into 120 c.c. of hot water, and the precipitated porphyrazine filtered off, washed, and dried; yield, 0·47 g. of a blue-black powder (Found: C, 81·5; H, 4·3; N, 11·7; *M*, in camphor, 890, 930. $C_{64}H_{40}N_8Mg$ requires *M*, 944).

Magnesium octaphenylporphyrazine is slightly soluble in alcohol, more easily in chloroform, benzene, acetone and *cyclo*hexanone, and readily in pyridine and quinoline. The solutions are emerald-green with a magnificent red fluorescence, destroyed by acids and heat. It separated from benzene as a microcrystalline powder, but could not be obtained macrocrystalline. Like other compounds of the series, it could not be sublimed in a vacuum and the m. p. was very high and indefinite. The solution in sulphuric acid was intensely violet, and on dilution with ice gave sulphonated metal-free derivatives. Attempted quantitative oxidation with acid ceric sulphate (Dent, Linstead and Lowe, J., 1934, 1038) gave no useful results.

A solution of 500 mg. of the magnesium compound in 50 c.c. of pyridine was boiled with a solution of an equal weight of anhydrous oxalic acid in a little pyridine. The colour rapidly changed through olive-green to brown and a solid was deposited. After a few minutes the solution was cooled, and the oxalate collected and washed with water; yield, 320 mg. of an insoluble black crystalline powder. Reconversion of the salt into its components is effected quantitatively by hot aqueous alkali carbonate and to a small extent by a large excess of boiling pyridine. The regenerated pigment still contains its magnesium. A similar series of reactions is effected by the use of acetic acid.

500 Mg. of magnesium octaphenylporphyrazine were boiled for 2 hours with 100 c.c. of 85% formic acid. Dilution of the brownish-green solution yielded a brown solid, which was washed thoroughly with pyridine and water and dried. *Octaphenylporphyrazine diformate* formed a brownish-black, crystalline, almost insoluble powder, which was free from magnesium (Found:

C, 77·8; H, 4·3; N, Kjeldahl, 11·7. $C_{64}H_{42}N_8,2H_2CO_3$ requires C, 77·9; H, 4·5; N, 11·1%). Treatment of the salt with caustic alkali gave the free porphyrazine, easily detected by its solubility in pyridine and its intense colour, which was more conveniently prepared as follows: 500 Mg. of the magnesium compound were boiled for 3 hours with 100 c.c. of 15% hydrochloric acid; the greenish solid was filtered off and treated similarly for a further 3 hours. The solid was dried and dissolved in 250 c.c. of benzene, and a small amount of unchanged magnesium derivative separated by chromatographic adsorption on alumina. The magnesium compound was preferentially adsorbed. The main band was eluted with warm pyridine, the extract concentrated, and free *octaphenylporphyrazine* (I, R = Ph) precipitated by the addition of water (Found: C, 83·3; H, 4·65; N, 12·5. $C_{64}H_{42}N_8$ requires C, 83·3; H, 4·6; N, 12·2%). It resembles the magnesium compound in solubility and appearance, but the colour is less bright and the solutions do not appear to be fluorescent. Vacuum sublimation was impossible.

Copper Derivative.—5·0 G. of diphenylmaleinitrile were heated at 275° with 0·5 g. of copper-bronze (more reactive than reduced copper) for 15 minutes. The solidification of the melt and the development of a purple reflex were similar to but less marked than those observed in the reaction with magnesium. The product was finely ground and extracted from unreacted metal with boiling pyridine. The pyridine solution was concentrated to 60 c.c. and poured into 200 c.c. of boiling water, and the precipitated *copper octaphenylporphyrazine* was filtered off, washed and dried (4·2 g.). Subsequent analyses showed this product to be pure, but as a precaution it was subjected to chromatographic adsorption. A solution of 0·5 g. in 300 c.c. of benzene gave a broad green band when passed through a 1·5 × 20 cm. column of alumina. This was eluted with pyridine, and the pigment precipitated as before and crystallised from benzene, yielding a greenish-black crystalline powder (Found: C, 78·2; H, 4·2; N, 11·1; Cu, 6·9, 6·5; *M*, in camphor, 950. $C_{64}H_{40}N_8Cu$ requires C, 78·1; H, 4·1; N, 11·4; Cu, 6·5%; *M*, 983). Copper was determined by oxidation with a mixture of nitric and sulphuric acids, followed by iodometric titration.

The metal in this compound and that described below was very firmly bound, and not removed by the methods used for the magnesium compound. The colour was comparatively dull and the solution did not fluoresce. The compound was remarkably stable to acids and withstood fusion with caustic potash in the air.

4·0 G. of diphenylmaleinitrile reacted vigorously with cuprous chloride (1·0 g.) at 250°. Hydrogen chloride was evolved and the melt became red, then greenish-black, and finally solidified. After 15 minutes the product was isolated in the same way as the simple copper compound, except that the solid was finally isolated by evaporation of a chloroform solution, instead of by crystallisation from benzene. *Copper monochloro-octaphenylporphyrazine* formed shining black scales, giving green solutions, and was practically indistinguishable from the unchlorinated compound (Found: C, 75·5; H, 3·9; N, 10·8; Cl, 3·6; Cu, 6·6; *M*, in camphor, 1050, 970. $C_{64}H_{39}N_8ClCu$ requires C, 75·4; H, 3·8; N, 11·0; Cl, 3·5; Cu, 6·3%; *M*, 1018).

Nuclear-substituted Compounds.—Di-*p*-nitrophenylmaleinitrile, m. p. 268°, was prepared in 56% yield by Heller's method (*Annalen*, 1904, **332**, 258) from *p*-nitrophenylacetonitrile ("Organic Syntheses," **2**, 57).

The nitro-nitrile reacted with explosive violence with metallic copper at 280°. On the small scale a product was isolated showing the typical properties of the compounds already described and a colour and absorption spectrum almost identical with those of the unsubstituted pigment. 4·0 G. of dinitrophenylmaleinitrile were heated with 1 g. of magnesium for 3 hours at 280° and a further 3 hours at 300°. The finely ground product was freed from metal with dilute acetic acid, and precipitated from a pyridine solution with boiling water; yield, 1·8 g. It was purified by the chromatographic method in the manner already described. *Magnesium octa-*p*-nitrophenylporphyrazine* was finally isolated by evaporation of a benzene solution as a dark green powder, with a similar colour and spectrum to those of the un-nitrated magnesium compound. The solutions were not fluorescent (Found: C, 59·1; H, 2·7; N, 17·6; Mg, 1·7. $C_{64}H_{32}O_{16}N_{16}Mg$ requires C, 58·9; H, 2·5; N, 17·2; Mg, 1·8%).

Di-*p*-aminophenylmaleinitrile was prepared by Heller's method (*loc. cit.*). This compound is not very suitable for porphyrazine formation, as it sublimes without melting above 300°. Qualitative experiments with cuprous chloride, zinc chloride, litharge, magnesium and copper both alone and in the presence of inert solvents have so far given no evidence of the formation of a porphyrazine.

Oxidation of Magnesium Octaphenylporphyrazine.—To a solution of 500 mg. of the compound in 500 c.c. of warm acetone, finely powdered potassium permanganate was added with shaking. The first portions were quickly reduced and much more of the reagent was decomposed than that

required for a simple oxidative fission. The solution was left at room temperature with an excess of permanganate for 3 days, by which time the characteristic fluorescence in ultra-violet light had disappeared. The product was filtered off and decolorised with sulphur dioxide, and the solvent removed under reduced pressure. The acidic portion was separated by means of sodium bicarbonate as usual and purified by sublimation, benzoic acid being identified by m. p. and mixed m. p.

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190. *Phthalocyanines. Part XII. Experiments on the Preparation of Tetrabenzporphyrins.*

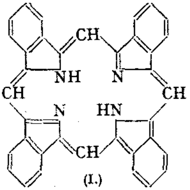
By R. P. LINSTEAD and E. G. NOBLE.

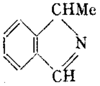
THE porphyrazines of Part XI (preceding paper) bridge one gap between phthalocyanines and porphyrins. The connection between the two series would be strengthened by the isolation of tetrabenzporphin (I) in which the pyrrole rings of porphin carry benzene rings fused to the β-carbon atoms. The close resemblance which this compound bears to phthalocyanine in molecular complexity would be expected to be reflected in a similarity in general properties, although differences in absorption spectra and basicity might be anticipated. This paper describes several unsuccessful attempts at its synthesis.

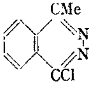
The methods elaborated by Hans Fischer for the synthesis of porphyrins all involve the use of substituted pyrroles or of dipyrrylmethenes, themselves prepared from pyrroles.

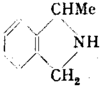
The corresponding parent ring system for the present investigation is the *iso*indole. The simple bases of this series are extremely unstable and formed with difficulty, if at all * (Gabriel and Neumann, *Ber.*, 1893, **26**, 521, 705, 952; Malan and Robinson, J., 1927, 2653; Fenton and Ingold, J., 1928, 3295).

The corresponding dihydro-compounds, although not very stable, are comparatively easily made (Gabriel and Neumann, *loc. cit.*; Scholtz and co-workers, *Ber.*, 1898, **31**, 414, etc.; von Braun and co-workers, *Ber.*, 1913, **46**, 1790; 1926, **59**, 2330) and many oxygenated derivatives such as phthalimide and phthalimidine are stable substances. A convenient starting material for the synthesis of tetrabenzporphin appeared to be available in the 1-methyl-ψ-*iso*indole (II) of Gabriel and Neumann (*loc. cit.*, p. 709). It was hoped that the methyl groups of this would supply the four linking methene groups of (I).


(I.)


(II.)


(III.)


(IV.)

A difficulty, however, arose in the preparation of the base. Gabriel and Neumann reported that 4-chloro-1-methylphthalazine (III), on reduction with zinc and hydrochloric acid,

* In an attempt to confirm the presence of the *iso*indole ring in phthalocyanine we distilled this with zinc dust. The products were benzonitrile, phthalonitrile, and ammonia. Indications of the presence of a trace of an *iso*indole base were obtained. The experiment resembles somewhat those of Gabriel (*Ber.*, 1880, **13**, 1685) and Bamberger (*ibid.*, 1888, **21**, 1888) on the zinc dust distillation of phthalimide, which yielded a trace of an *iso*indole base, probably a dihydro-base.

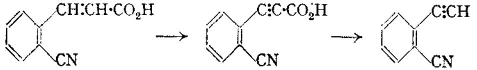
yielded 1-methyl-ψ-*iso*indole (II), whereas the use of tin and hydrochloric acid carried reduction to the dihydro-stage (IV). The parent base (II) was characterised and analysed by them as the double zinc chloride, the platinichloride, and the picrate, the dihydro-base (IV) as the hydrochloride (m. p. 170°) and nitrosoamine (m. p. 98°).

Fenton and Ingold (*loc. cit.*), who used the same preparative methods, describe the picrate of (II) as decomposing from 135° upwards, and the picrate of the dihydro-base as melting at 151°. We have carefully repeated these reductions and can find no evidence for the formation of methyl-ψ-*iso*indole. In our hands the product from the reduction of 4-chloro-1-methylphthalazine by both of Gabriel's methods was the dihydro-base (IV) and yielded the same hydrochloride (m. p. 170°), methiodide (m. p. 125°), and nitrosoamine (m. p. 100°). The picrate of the base made by reduction with zinc melted at 150°. Mixtures of the derivatives of the base made by the two methods showed no depression of melting point. Gabriel's analytical figures were obtained with derivatives containing large added groups and the effect of the two atoms of hydrogen was masked. Our analyses of the free base, made by zinc reduction, corresponded with those required for the dihydro-compound. Moreover, the base, however prepared, was extracted from a petroleum solution by aqueous sodium dihydrogen phosphate. By analogy with Willstätter's work, this would be expected of the dihydro-base, but not of methyl ψ-*iso*indole itself. It may also be pointed out that Gabriel and Neumann (*loc. cit.*, p. 526) themselves showed that the reduction of 4-chlorophthalazine with zinc and hydrochloric acid yielded dihydro*iso*indole and not ψ-*iso*indole itself. There seems no reason why the methyl group should modify the course of this reduction.

The reduction of 4-chloro-1-methylphthalazine by metal and acid therefore gives methyldihydro*iso*indole.* Similarly, Fenton and Ingold (*loc. cit.*) observed that alkaline degradation of the *p*-toluenesulphonyl derivatives of dihydro*iso*indoles yielded not the expected ψ-*iso*indoles but their dihydro-derivatives. There therefore appears to be no valid evidence for the existence of ψ-*iso*indole and its simple (unreduced) derivatives, and the abrupt contrast with pyrrole is of considerable theoretical interest (Ingold, J., 1933, 1127).

There seemed a speculative possibility of converting 1-methyldihydro*iso*indole into a tetrabenzporphyrin by direct oxidation of the base or its salts, particularly in the presence of metals capable of yielding complex metallic compounds. The base is indeed very readily oxidised, even by atmospheric oxygen—it cannot be isolated by evaporation of its solutions in organic solvents without special precautions—but no products of the desired type could be prepared in this way. Attempts were therefore made to effect the oxidation indirectly by bromination, followed by elimination of hydrogen bromide. The only recognisable product obtained in this way was 1-*methyldihydro*isoindole *hydrobromide*.

We also examined the action of metallic reagents on o-*cyanophenylacetylene* (V), which from its structural resemblance to phthalonitrile might be expected to reproduce the exceptional reactivity of this compound. It was made by decarboxylating *o*-cyanophenylpropiolic acid (VI), itself prepared from the *dibromide* of *o*-cyanocinnamic acid (VII).



(VII.) (VI.) (V.)

Neither the cyano-acetylene (V) nor the acids of associated structure, however, reacted with metallic reagents in the desired way. The acetylene (V) also failed to condense with its own copper derivative.

Many of the attempts described above gave very intractable products. Hence it is not possible to exclude the formation of tetrabenzporphyrins with complete certainty. Nevertheless it is clear that there is no pronounced tendency for their formation from the

* Professor C. K. Ingold, to whom these facts were communicated privately, agrees that there is now no reason to suppose that the two bases obtained in the earlier work were not the dihydro-compounds in different degrees of purity. The new facts rather strengthen than otherwise the general inferences in Fenton and Ingold's paper.

intermediates mentioned in this paper, in any way comparable with that which is shown for the preparation of phthalocyanines.

EXPERIMENTAL.

1-*Methyldihydro*iso*indole and Related Compounds.*—A solution of 30 g. of 4-chloro-1-methylphthalazine (Gabriel and Neumann, *Ber.*, 1893, **26**, 705, 952) in 200 c.c. of 20% hydrochloric acid was treated during 30 minutes with 50 g. of zinc turnings, after the addition of 5 c.c. of concentrated hydrochloric acid the mixture was kept for an hour, then made strongly alkaline with 130 g. of caustic soda in 50% solution and distilled in steam. The distillate was extracted with purified light petroleum (b. p. 40—60°), the extract dried over anhydrous potassium carbonate, and the solvent removed in an atmosphere of nitrogen. The residue was distilled under reduced pressure in a current of nitrogen. Access to the air was avoided as far as possible, nitrogen being admitted to the apparatus when the receivers were changed. A repeatable yield of 9 g. (40%) of methyldihydro*iso*indole, b. p. 94°/6 mm., 102°/15 mm., was obtained (Found: C, 80·9; H, 8·2. Calc. for $C_9H_{11}N$: C, 81·2; H, 8·3%. Calc. for C_9H_9N: C, 82·5; H, 6·9%). For this analysis, the freshly distilled base was transferred rapidly to a nitrogen-filled bulb. The free base and its solutions rapidly turned red when exposed to the air. If ether was used as an extracting solvent in place of petroleum and no nitrogen was used during its removal, the dark red viscous residue contained none of the base, owing to oxidation, probably through the action of peroxide in the ether.

The *hydrochloride*, m. p. 170°, was best obtained by passing dry hydrogen chloride over the ice-cold base in the absence of air, and removing the excess of base by rubbing with light petroleum (Found: Cl, 20·75. $C_9H_{11}N$,HCl requires Cl, 20·95%). The reaction did not proceed so well in aqueous or alcoholic solution. The base readily reacted with alkyl halides either alone or in alcoholic or petroleum solution. The compounds with ethyl iodide and ethyl bromide melted respectively at 152° and 150°.

4-Chloro-1-methylphthalazine (25 g.) was heated on the steam-bath with an excess of tin and concentrated hydrochloric acid (250 c.c.) for 4 hours, and for another 4 hours after the addition of more acid (100 c.c.). The product, worked up in the manner described for the reduction with zinc, yielded 7 g. (38%) of methyldihydro*iso*indole, b. p. 108—110°/25 mm. This gave a hydrochloride, m. p. 170°, methiodide, m. p. 126°, and nitrosoamine, m. p. 100°, the m. p.'s of which were not depressed by admixture with the corresponding derivatives of the zinc reduction product.

1·5 G. of the base were completely removed from its solution in 25 c.c. of petroleum (b. p. 40—60°) by extraction with 25 c.c. of water containing 10 g. of sodium dihydrogen phosphate. The base could be recovered by making the aqueous solution alkaline and extracting it with petroleum.

Reactions with Oxidising Agents and Metals.—After methyldihydro*iso*indole had been distilled, particularly under oxidising conditions, a reddish-brown semi-solid residue remained. This yielded a purple solution in acid which deposited a precipitate on basification. After extraction with benzene and evaporation the solid yielded a reddish-brown intractable powder containing about 13% of oxygen (Found: C, 71·9; H, 6·6; N, 8·2%). A similar product was obtained by oxidation of the base in aqueous solution. Red oxidation products were also formed from the interaction of the base and cuprous chloride, and with anhydrous cupric and ferric chlorides. Zinc chloride in β-methylnaphthalene gave a purplish-blue colour at 80—120°, but no definite coloured compound could be isolated.

After a number of preliminary experiments with bromine, a crystalline product was obtained in the following way. A solution of 10·5 g. of methyldihydro*iso*indole in 52 c.c. of glacial acetic acid was treated slowly in ice with 13·5 g. of bromine dissolved in 53 c.c. of glacial acetic acid. The mixture was kept for an hour, and the solvent removed over alkali in a vacuum desiccator. The crystalline product was drained on a porous tile, and a highly brominated impurity removed by Soxhlet extraction with petroleum. This contained 50·7% of bromine, probably partly in the nucleus. The residue, which was very soluble in alcohol and water, was crystallised twice by evaporating its aqueous solution. It formed long needles, m. p. 160°, and was identified as 1-*methyldihydro*iso*indole hydrobromide* by analysis (Found: Br, 37·6. $C_9H_{11}N$,HBr requires Br, 37·4%) and by conversion into the base (nitrosoamine, m. p. and mixed m. p. 98°).

Degradation of Phthalocyanine.—An intimate mixture of 4 g. of pure phthalocyanine and 20 g. of zinc dust was heated cautiously in a current of nitrogen. At a bath temperature of 270—350°, a red deposit formed on the cold parts of the tube. At 350—470° a small quantity of a crystalline sublimate (phthalonitrile) was formed. There was little decomposition, however, until the mixture was heated to dull redness with a free flame; ammonia, benzonitrile—identified by

hydrolysis to benzoic acid—and phthalonitrile—identified by m. p., mixed m. p., and conversion into sodium phthalocyanine—were then evolved freely. The red deposit first formed probably corresponded to the formation of a trace of an *iso*indole derivative, but could not be obtained in quantity sufficient for examination.

o-*Cyanophenylacetylene* (V).—*o*-Cyanocinnamic acid (VII) was prepared by isomerisation of the sodium salt of α-nitroso-β-naphthol in boiling nitrobenzene, essentially by the method of Davies and Poole (J., 1927, 2661). It was found convenient to dry the acid first by azeotropic distillation with benzene (5 vols.) and finally over sulphuric acid in a vacuum desiccator. It formed leaflets, m. p. 255°, from alcohol (yield, 40%). Ethyl phthalate and naphthalene were far inferior as media for the isomerisation, giving yields of only about 20%. The preparation of this acid from *o*-aminocinnamic acid or its ethyl ester by the Sandmeyer reaction was much less satisfactory. The acid was left in the dark in a desiccator over an equal weight (slight excess) of bromine. After 3 days the vapour was completely absorbed and the *dibromide* was freed from adsorbed bromide in a vacuum desiccator. It was a yellow powder, m. p. 184—186° (decomp.) (Found: Br, 47·9. $C_{10}H_7O_2NBr_2$ requires Br, 48·1%).

Several methods were tried for the complete debromination of this compound, but under the optimum conditions the desired *o*-cyanophenylpropiolic acid (VI) was always contaminated with a large amount of 1-*bromo*-2-o-*cyanophenylacrylic acid*. The mixture could, however, be used for the preparation of *o*-cyanophenylacetylene. The best results were obtained as follows: 10 g. of the dibromo-acid were kept for 8 hours with 10% aqueous potassium hydroxide (2½ equivs.). The recovered acid, which contained bromide, was similarly treated for a further 24 hours, and the acid was again regenerated and finally treated with 25% caustic potash solution (2½ equivs.) for 24 hours. After regeneration and crystallisation from benzene it had m. p. 140—142° and an equivalent weight 228·2, corresponding to about 70% of the monobromo-acid. 20% Aqueous caustic soda gave a similar result, and alcoholic potash a rather worse one. Heating resulted in hydrolysis of the cyano-group. The 1-bromo-2-*o*-cyanophenylacrylic acid was isolated from the mixtures by crystallisation from water. It formed needles, m. p. 156—158° (Found: N, 5·85; equiv., 249·5. $C_{10}H_6O_2NBr$ requires N, 5·6%; equiv., 252).

The mixture of acids, containing 25—30% of *o*-cyanophenylpropiolic acid, was boiled under reflux for 24 hours with 10 vols. of water, and the product distilled in steam, the same condenser, which already contained some of the acetylene, being used. o-*Cyanophenylacetylene* separated from the distillate and more was obtained by extraction with ether. It formed white needles, m. p. 76° (Found: N, 11·0. C_9H_5N requires N, 11·0%). The yield was only 25% allowing for the impurity in the starting material, and much resin was formed. The product formed a white silver and a yellow copper derivative by the usual methods.

Attempts to prepare *o*-cyanophenylacetylene from *o*-aminophenylacetylene (v. Baeyer and Landsberg, *Ber.*, 1882, **15**, 60; v. Baeyer and Bloem, *Ber.*, 1884, **17**, 964) yielded only tarry products.

o-Cyanophenylacetylene and the mixture of *o*-cyanophenylpropiolic acid and bromocyanophenylacrylic acid yielded no sign of the formation of a stable pigment when heated under the usual conditions with the following reagents, there being only gross decomposition: metallic sodium, sodium ethoxide and amyloxide, magnesium metal and oxide, copper and both its chlorides, zinc chloride, ferric chloride.

The following related intermediates were prepared for testing for the formation of simple phthalocyanines (compare J., 1934, 1034). *o*-Cyanocinnamic acid was converted into the acid chloride in 78% yield by the action of thionyl chloride in benzene. This formed needles, m. p. 95°, from light petroleum, and with ammonia gas in benzene yielded *o*-cyanocinnamamide, m. p. 203—204° (Gabriel, *Ber.*, 1916, **49**, 1608). When this was heated under reduced pressure with an equal weight of phosphoric oxide (bath at 220°), o-*cyanocinnamonitrile* distilled, b. p. 173—174°/5 mm., m. p. 108°; yield, 55% (Found: N, 18·4. $C_{10}H_6N_2$ requires N, 18·2%). The following were made by Gabriel's methods: Phthalazone (*Ber.*, 1893, **26**, 521); phthalazine from 4-chlorophthalazine (*Ber.*, 1897, **30**, 3022) and from ωω'-bisdibromo-*o*-xylene (*Ber.*, 1893, **26**, 2210; 1895, **28**, 1830); 1-methylphthalazone (*Ber.*, 1893, **26**, 952). None of these yielded phthalocyanines on treatment with the reagents described in the preceding paragraph.

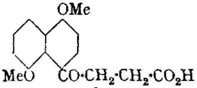
We thank Imperial Chemical Industries, Ltd. (Research Council), for a grant and for gifts of chemicals.

Imperial College of Science and Technology,
London, S.W. 7. [*Received, April 15th, 1937.*]

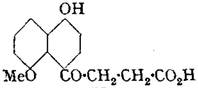
191. *Syntheses in the Phenanthrene Series. Part VII.* 5 : 9-*Dimethoxy- and* 5-*Methoxy*-1-*methylphenanthrene.*

By Peter Hill, W. F. Short, and H. Stromberg.

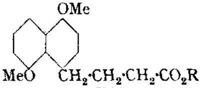
Condensation of 1 : 5-dimethoxynaphthalene with succinic anhydride in presence of aluminium chloride furnished an acid, $C_{16}H_{16}O_5$, m. p. 173·5—174°, which must be β-(4 : 8-*dimethoxy*-1-*naphthoyl*)*propionic acid* (I), since it was also obtained from succinic anhydride and the Grignard compound of 4-bromo-1 : 5-dimethoxynaphthalene (see below). In tetrachloroethane solution a smooth reaction occurred at 70° and gave an 80% yield of an *acid*, $C_{15}H_{14}O_5$, m. p. 184°. This acid afforded (I) in excellent yield on methylation and, owing to its yellow colour, we ascribe to it formula (II). Reduction of the keto-acid (I) presented considerable difficulty owing to the ease with which the side chain was removed from the molecule (compare Hill and Short, J., 1935, 1123). By using an active zinc amalgam, esterifying the product, and separating 1 : 5-dimethoxynaphthalene by distillation, a 20% yield of *methyl* γ-(4 : 8-*dimethoxy*-1-*naphthyl*)*butyrate* (III; R = Me) was obtained.



(I.)

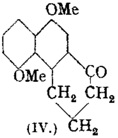


(II.)



(III.)

Dehydration of the *acid* (III; R = H) was effected with phosphoric oxide and the resulting 1-*keto*-5 : 9-*dimethoxy*-1 : 2 : 3 : 4-*tetrahydrophenanthrene* (IV) afforded 5 : 9-*dimethoxy*-1-*methyl*-3 : 4-*dihydrophenanthrene* on treatment with methylmagnesium iodide. Dehydrogenation with palladium–charcoal furnished 5 : 9-*dimethoxy*-1-*methylphenanthrene* (V), m. p. 139—140°. Oxidation of (V) under a variety of conditions produced red amorphous substances and no 5-methoxy-1-methylphenanthra-9 : 10-quinone could be isolated.



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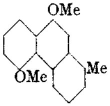

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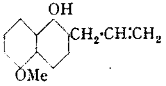
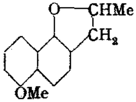
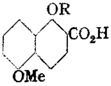


(VI.)

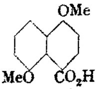
In order to establish the formula of the keto-acid (I), 5-methoxy-1-naphthol was first converted into its *allyl* ether and rearranged to 5-*methoxy*-2-*allyl*-1-*naphthol* (VI), the structure of which was determined by conversion into the *coumaran* derivative (VII). The naphthol (VI) was cryptophenolic, but could be methylated in Claisen's potash. Oxidation of the methyl ether afforded 1 : 5-*dimethoxy*-2-*naphthoic acid* (VIII; R = Me). 1-*Hydroxy*-5-*methoxy*-2-*naphthoic acid* (VIII; R = H) was obtained in excellent yield from 5-methoxy-1-naphthol by the Kolbe reaction. The hydroxyl group of this acid resisted methylation, and an excess of diazomethane produced a mixture of the *methyl* esters of 1-hydroxy-5-methoxy- and 1 : 5-dimethoxy-2-naphthoic acid.



(VII.)



(VIII.)

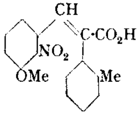


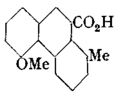
(IX.)

The orientation of 1 : 5-dimethoxy-2-naphthoic acid establishes the formula of the bromo-1 : 5-dimethoxynaphthalene prepared by Fischer and Bauer (*J. pr. Chem.*, 1916, **94**, 15), since

carbonation of its Grignard reagent afforded the isomeric 4 : 8-*dimethoxy*-1-*naphthoic acid* (IX). The formulæ assigned to the isomeric aldehydes produced by the application of the Gattermann reaction to 1 : 5-dihydroxynaphthalene (Gattermann, *Annalen*, **1907**, **357**, **341**; Morgan and Vining, J., 1921, **119**, 177) and by the hydrolysis of 5-hydroxy-1-keto-2-indoxyl-1 : 2-dihydronaphthalene (Bezdzik and Friedländer, *Monatsh.*, 1909, **30**, 286) are based on their physical properties and on the assumption that a derivative of α-naphthol would undergo substitution in position 4 in the Gattermann synthesis. Oxidation of the *methyl* ethers of these aldehydes gave the acids (IX) and (VIII) respectively, so that the structures assigned to them by the earlier workers are confirmed.

For the synthesis of 5-*methoxy*-1-*methylphenanthrene*, *o*-allyltoluene (Hurd and Bollman, *J. Amer. Chem. Soc.*, 1934, **56**, 447) was oxidised to *o*-tolylacetic acid by the method described in Part IV (this vol., p. 260), and the potassium salt of this acid condensed with 2-nitro-3-methoxybenzaldehyde (Rieche, *Ber.*, 1889, **22**, 2349). The resulting 2-*nitro*-3-*methoxy*-α-o-*tolylcinnamic acid* (X) was reduced to the *amino-acid* and converted into 5-*methoxy*-1-*methylphenanthrene*-10-*carboxylic acid* (XI) by diazotisation and warming with alkali. The acid (XI) was decarboxylated by heating with quinoline and copper powder.

(X.) 

 (XI.)

EXPERIMENTAL.

β-(4 : 8-*Dimethoxy*-1-*naphthoyl*)*propionic Acid* (I).—(1) Powdered succinic anhydride (44 g.) and 1 : 5-dimethoxynaphthalene (Bentley, Robinson, and Weizmann, J., 1907, **91**, 106) (83 g.) were added with shaking to an ice-cold solution of aluminium chloride (118 g.) in nitrobenzene (360 c.c.). The mixture was slowly warmed to room temperature with stirring and then kept for 190 hours. The *keto-acid*, isolated in the usual way (85% yield), separated from methyl alcohol in small rods, m. p. 173·5—174° (Found: C, 66·4; H, 5·7. $C_{16}H_{16}O_5$ requires C, 66·7; H, 5·6%). The *methyl* ester separated from methyl alcohol in leaflets, m. p. 91—92° (Found: C, 67·6; H, 6·1. $C_{17}H_{18}O_5$ requires C, 67·6; H, 5·9%). Nitrobenzene is an unsuitable solvent for the preparation of large quantities of this acid, since an uncontrollable oxidation is liable to occur. When the condensation was effected in boiling carbon disulphide, a 21% yield of the keto-acid was obtained in 9 hours. (2) A Grignard solution prepared from 4-bromo-1 : 5-dimethoxynaphthalene (1 mol.), magnesium (1 atom), and ether (5 mols.) was added during ¾ hour to a boiling suspension of finely powdered succinic anhydride (1 mol.) in ether (17 mols.) and after boiling for 2 hours the yellow complex was decomposed with ice-cold, dilute sulphuric acid. The acid was extracted from the solvent with dilute sodium carbonate solution and purified by crystallisation from methyl alcohol; m. p. 173—174° (yield, 25%). Esterification with methyl-alcoholic hydrogen chloride afforded the methyl ester, m. p. and mixed m. p. 91—92°.

β-(4-*Hydroxy*-8-*methoxy*-1-*naphthoyl*)*propionic Acid*.—Powdered aluminium chloride (2·7 mols.) was added in portions to succinic anhydride (1 mol.), 1 : 5-dimethoxynaphthalene (1 mol.), and tetrachloroethane (10 mols.) at 40°, and the mixture slowly warmed to 74° (4 hours). The *keto-acid*, isolated in the usual way, crystallised from methyl alcohol in long yellow plates, m. p. 184° (decomp.) (Found: C, 65·75; H, 5·25. $C_{15}H_{14}O_5$ requires C, 65·7; H, 5·1%). Methylation in 3*N*-sodium hydroxide (2·5 mols.) with methyl sulphate (1·5 mols.) at 35—60° afforded β-(4 : 8-dimethoxy-1-naphthoyl)propionic acid in quantitative yield.

γ-(4 : 8-*Dimethoxy*-1-*naphthyl*)*butyric Acid*.—The keto-acid (I) was not reduced by prolonged boiling with zinc or copper–zinc in presence of aqueous sodium hydroxide and ammonia, and after numerous trials the following method was devised. 460 G. of zinc dust were amalgamated (2—3 minutes) with 400 c.c. of 5% mercuric chloride solution, the liquid decanted, and a hot solution of the keto-acid (100 g.) in acetic acid (800 c.c.) added to the amalgam. The mixture was boiled and 600 c.c. of concentrated hydrochloric acid were added during 7—10 minutes, and the mixture boiled for 1 hour. After most of the acetic acid had been removed in steam, the liquid was filtered, and the organic material separated from the excess of zinc by extraction with ether. The solution was dried and evaporated, and the residue dissolved in concentrated methyl-

alcoholic hydrogen chloride (600 c.c.). After boiling for 2 hours the crude ester was collected in the usual way and distilled. Fraction (1), b. p. up to 216°/0·8 mm., consisted of 1 : 5-dimethoxynaphthalene; fraction (2), b. p. 216—225°/0·8 mm., solidified on cooling, and there was a considerable resinous residue. Crystallisation of fraction (2) from ice-cold methyl alcohol or light petroleum (b. p. 40—60°) furnished *methyl γ-(4 : 8-dimethoxy-1-naphthyl)butyrate* in glistening plates, m. p. 67—67·5° (Found : C, 70·9; H, 7·05. $C_{17}H_{20}O_4$ requires C, 70·8; H, 6·9%). Saponification with alcoholic potash gave the *acid* (III), which crystallised from acetic acid in rounded hexagons, m. p. 154° (Found : C, 69·9; H, 6·6. $C_{16}H_{18}O_4$ requires C, 70·1; H, 6·6%). The overall yield was 20%.

1-*Keto*-5 : 9-*dimethoxy*-1 : 2 : 3 : 4-*tetrahydrophenanthrene*.—Phosphoric oxide (15 g.) was added in portions with shaking to a boiling solution of the acid (III) (3 g.) in benzene (50 c.c.), and the mixture was boiled for 3 hours, decomposed with ice, and repeatedly extracted with ether. The solvent layer was washed with dilute sodium carbonate solution to remove unchanged acid (0·9 g.), dried, and evaporated. Crystallisation of the residue from alcohol (charcoal) gave the cyclic *ketone* (1·9 g.) in long, colourless plates, m. p. 124° (Found : C, 75·0; H, 6·3. $C_{16}H_{16}O_3$ requires C, 75·0; H, 6·2%). The 2 : 4-*dinitrophenylhydrazone* was a crimson microcrystalline powder, m. p. 295° (decomp.) (Found : N, 12·9. $C_{22}H_{20}O_6N_4$ requires N, 12·8%).

5 : 9-*Dimethoxy*-1-*methyl*-3 : 4-*dihydrophenanthrene*.—A solution of the preceding cyclic ketone (4·6 g.) in dry benzene (50 c.c.) was added to an ice-cold solution of methylmagnesium iodide (from methyl iodide, 1·8 c.c., magnesium, 0·65 g., and ether, 20 c.c.), and the mixture boiled for 1 hour. The complex was decomposed in the usual way, and the product distilled. The main fraction (3·4 g.), b. p. 220—230°/0·9 mm., consisted of the unsaturated compound with a little unchanged ketone, and a fraction (0·7 g.) of higher b. p. of unchanged ketone. The mixture was separated by crystallisation from absolute alcohol, 5 : 9-*dimethoxy*-1-*methyl*-3 : 4-*dihydrophenanthrene* being obtained in colourless plates, m. p. 111—111·5° (Found : C, 80·0; H, 6·75. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%).

5 : 9-*Dimethoxy*-1-*methylphenanthrene*.—Dehydrogenation of the dihydro-compound was effected by heating at 300—330° for 2 hours with 10% palladium–charcoal (0·6 part), and the product purified by crystallisation. 5 : 9-*Dimethoxy*-1-*methylphenanthrene* separated from absolute alcohol in thin, irregular plates, m. p. 139—140° (Found : C, 81·5; H, 6·3. $C_{17}H_{16}O_2$ requires C, 80·95; H, 6·3%). The *picrate* consisted of crimson needles, m. p. 200° (Found : C, 57·3; H, 3·9. $C_{17}H_{16}O_2,C_6H_3O_7N_3$ requires C, 57·4; H, 3·95%).

5-*Methoxy*-1-*naphthyl Allyl Ether*.—A mixture of 5-methoxy-1-naphthol (Fischer and Bauer, *J. pr. Chem.*, 1916, **94**, 15) (27·4 g.), acetone (34 c.c.), allyl bromide (14·8 c.c.), and potassium carbonate (26 g.) was boiled gently under reflux for 19 hours. The product was shaken with hot water, and the light brown solid dissolved in ether, washed with sodium hydroxide solution to remove unchanged naphthol (3·3 g.), dried, and evaporated. Recrystallisation of the residue from ligroin (charcoal) gave colourless plates of the *allyl* ether, m. p. 103° (Found : C, 78·7; H, 6·45. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·5%). This compound was insoluble in Claisen's potash (*Annalen*, 1926, **449**, 86) and did not couple with benzenediazonium chloride. The yield was 55% and a liquid cryptophenolic by-product was formed.

5-*Methoxy*-2-*allyl*-1-*naphthol*.—The preceding allyl ether was heated at 240° (oil-bath) under a pressure of 22 mm. for 1½ hours and then distilled. The distillate, b. p. 200—202°/9 mm., crystallised from light petroleum (b. p. 60—80°) in slightly coloured, long rods, m. p. 82—83° (Found : C, 78·6; H, 6·5. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·5%). 5-*Methoxy*-2-*allyl*-1-*naphthol* is insoluble in 5*N*-sodium hydroxide, but dissolves in Claisen's potash. Yield, 73%.

1 : 5-*Dimethoxy*-2-*allylnaphthalene*.—Addition of methyl sulphate (54 c.c.) to a solution of the naphthol (4·6 g.) in Claisen's potash (124 c.c.) with occasional cooling afforded a 75% yield of the *methyl* ether, b. p. 186—187°/10 mm., which separated from ice-cold methyl alcohol in colourless plates, m. p. 24—25° (Found : C, 78·8; H, 7·1. $C_{15}H_{16}O_2$ requires C, 79·0; H, 7·0%). Oxidation of this compound with 3% aqueous potassium permanganate (equivalent to 5 atoms of oxygen) produced 1 : 5-*dimethoxy*-2-*naphthoic acid* (below), which was identified as its methyl ester.

5-*Methoxy*-1-*methyl*-1 : 2-*dihydro*-α-*naphthafuran*.—5-Methoxy-2-allyl-1-naphthol and ⅛th of its weight of dry pyridine hydrochloride were heated at 220° (oil-bath) for 2—3 minutes in an atmosphere of nitrogen, and the mixture poured into hot water and washed by decantation. The solid was triturated with Claisen's potash, and washed with water. Extraction with hot methyl alcohol removed a black, sparingly soluble oil and the product was purified by successive crystallisations from 60% alcohol (charcoal) and methyl alcohol. The *coumaran* derivative

formed colourless, rectangular plates, m. p. 116°, and was phototropic (Found: C, 78·4; H, 6·5; *M*, Rast, 210. $C_{14}H_{14}O_2$ requires C, 78·5; H, 6·5%; *M*, 214).

1-*Hydroxy-5-methoxy-2-naphthoic Acid*.—An intimate mixture of 5-methoxy-1-naphthol and potassium bicarbonate (2 parts) was heated for 3 hours in a sealed tube at 220°, and the product dissolved in a large volume of water and filtered from a small amount of resin. Acidification of the filtrate precipitated the *acid* (yield, over 90%), which separated from methyl alcohol in white crystals which rapidly turned yellow on exposure to light, m. p. 212·5—213° (decomp.) (Found: C, 66·2; H, 4·6. $C_{12}H_{10}O_4$ requires C, 66·1; H, 4·6%).

1 : 5-*Dimethoxy-2-naphthoic Acid*.—(1) An ethereal solution of diazomethane (2·5 mols.) was added to a suspension of the preceding acid in dry ether, kept for 160 hours, and evaporated to dryness, and the residue recrystallised from methyl alcohol. A small crop of crystals (A) was removed, the filtrate evaporated, and the residue recrystallised from chloroform–light petroleum (b. p. 60—80°), giving elongated plates of *methyl* 1 : 5-*dimethoxy-2-naphthoate*, m. p. 80—81° (Found: C, 68·2; H, 5·7. $C_{14}H_{14}O_4$ requires C, 68·3; H, 5·7%). Hydrolysis with alcoholic potash afforded 1 : 5-*dimethoxy-2-naphthoic acid*, which separated from alcohol in clusters of small rods, m. p. 151—152° (Found: C, 67·1; H, 5·2. $C_{13}H_{12}O_4$ requires C, 67·2; H, 5·2%). Recrystallisation of (A) from benzene–light petroleum (b. p. 40—60°) furnished colourless plates, m. p. 118—119° (Found: C, 67·1; H, 5·2. $C_{13}H_{12}O_4$ requires C, 67·2; H, 5·2%). This compound was only slightly soluble in aqueous sodium hydroxide, and when Claisen's potash was added to a solution in ligroin, a white sodium salt was precipitated. Saponification afforded 1-hydroxy-5-methoxy-2-naphthoic acid, m. p. 212·5—213° (decomp.), so (A) must be *methyl* 1-*hydroxy-5-methoxy-2-naphthoate*. (2) 1 : 5-Dimethoxy-2-naphthaldehyde (Bezdzik and Friedländer, *loc. cit.*) was oxidised by the slow addition of warm 0·3% aqueous potassium permanganate (equivalent to 1 atom of oxygen), and the acid collected and recrystallised from alcohol. It melted at 151—152° alone and when mixed with the acid prepared by method (1).

4 : 8-*Dimethoxy*-1-*naphthoic Acid*.—(1) Solid carbon dioxide was added to a Grignard solution prepared from 4-bromo-1 : 5-dimethoxynaphthalene (1 mol.), magnesium (1 atom), and ether (5 mols.), and the acid isolated in the usual way. 1 : 5-*Dimethoxy-4-naphthoic acid*, obtained in 32% yield, crystallised from alcohol in hexagonal plates, m. p. 222·5° (decomp.) (Found: C, 66·9; H, 5·2. $C_{13}H_{12}O_4$ requires C, 67·2; H, 5·2%). Methylation with diazomethane gave a quantitative yield of the *methyl* ester, which crystallised from methyl alcohol in elongated plates, m. p. 173—173·5° (Found: C, 68·1; H, 5·7. $C_{14}H_{14}O_4$ requires C, 68·3; H, 5·7%). When the acid was boiled with hydrobromic–acetic acid, decarboxylation occurred and 1 : 5-dihydroxynaphthalene was formed. (2) Methylation of 4 : 8-dihydroxy-1-naphthaldehyde (Morgan and Vining, *loc. cit.*) with methyl sulphate (2 mols.) and 10% aqueous sodium hydroxide (2·3 mols.) furnished the *dimethyl* ether, which crystallised from methyl alcohol in colourless plates, m. p. 131—131·5° (Found: C, 72·3; H, 5·6. $C_{13}H_{12}O_3$ requires C, 72·2; H, 5·6%). Oxidation under the conditions specified for the isomeric aldehyde produced 4 : 8-dimethoxy-1-naphthoic acid (methyl ester, m. p. 173°) identical with that produced by method (1).

4 : 8-*Dihydroxy*-1-*naphthoic Acid*.—Cautious fusion of 4 : 8-dihydroxy-1-naphthaldehyde with potassium hydroxide (5 parts) at 180—200° produced 4 : 8-*dihydroxy*-1-*naphthoic acid*, which separated from ether–ligroin as a sandy, micro-crystalline powder, m. p. 213° (decomp.) (Found: C, 64·9; H, 4·3. $C_{11}H_8O_4$ requires C, 64·7; H, 3·9%). Methylation with methyl sulphate and alkali gave 4 : 8-dimethoxy-1-naphthoic acid, m. p. 219—220° (decomp.).

o-*Tolylacetic Acid*.—*o*-Allyltoluene, b. p. 83—85°/28 mm., obtained in 65% yield from *o*-tolylmagnesium iodide and allyl bromide (compare Hurd and Bollman, *loc. cit.*), was oxidised at 0° with 5% aqueous potassium permanganate (equivalent to 6 atoms of oxygen) and acetic acid (7·2 mols.). *o*-Tolylacetic acid, b. p. 165—170°/12 mm., m. p. 85—88°, isolated as in previous cases (this vol., p. 262), was obtained in 53% yield and 24% of *o*-allyltoluene was recovered.

2-*Nitro-3-methoxybenzaldehyde*.—The recorded methods for the nitration of *m*-methoxybenzaldehyde (Rieche, *loc. cit.*; Friedländer and Scheiber, *Ber.*, 1895, **28**, 1385; Hodgson and Beard, J., 1926, 154; 1927, 2380; Tröger and Sabewa, *J. pr. Chem.*, 1927, **117**, 124) are conflicting; the following method gave reproducible results and was applied to the nitration of 20—50 c.c. batches of the aldehyde. *m*-Methoxybenzaldehyde (20 c.c.) was added in one portion with shaking to 85% nitric acid (*d* 1·48; 79 c.c., previously freed from nitrous acid by addition of 2·5 g. of urea) cooled below − 1°. The temperature was then allowed to rise slowly, but was prevented from exceeding 24—25° by occasional cooling. After 30—35 minutes, the mixture was poured into ice-water, and the solid was collected, washed with water, dried, and dissolved in hot benzene (17 c.c.). The crystals deposited on cooling were recrystallised from acetic acid

(46 c.c.) and melted at 102° (yield, 26%). By extracting the solid obtained from the benzene and acetic acid mother-liquors with hot ligroin and recrystallising the sparingly soluble portion from acetic acid, a further quantity of the aldehyde was isolated (total yield, 30%).

2-Nitro-3-methoxy-α-o-tolylcinnamic Acid.—This acid was obtained in 56% yield by heating dry potassium *o*-tolylacetate (1 mol.), 2-nitro-3-methoxybenzaldehyde (1 mol.), and acetic anhydride (10 mols.) on the steam-bath for 27 hours. Recrystallisation from acetic acid afforded slightly coloured, well-defined, octahedral crystals, m. p. 220° (Found: N, 4·4. $C_{17}H_{15}O_5N$ requires N, 4·5%).

2-Amino-3-methoxy-α-o-tolylcinnamic Acid.—Reduction of the preceding acid with ferrous sulphate (7·7 mols.) and ammonia, and crystallisation of the product from benzene, afforded the *amino-acid* in clusters of yellow needles, m. p. 205—206° (Found: C, 71·9; H, 6·0. $C_{17}H_{17}O_3N$ requires C, 72·1; H, 6·0%).

5-Methoxy-1-methylphenanthrene-10-carboxylic Acid.—A suspension of the amino-acid in excess of dilute sulphuric acid (5%) was stirred at 50° and diazotised with sodium nitrite (1·8 mols.), during ½ hour. The mixture was made alkaline, warmed at 90° for a few minutes, and filtered hot. Acidification of the filtrate and recrystallisation of the precipitate from acetic acid gave a 43% yield of *5-methoxy-1-methylphenanthrene-10-carboxylic acid*, which crystallised in large, colourless plates, m. p. 224—225° (Found: C, 76·5; H, 5·3. $C_{17}H_{14}O_3$ requires C, 76·7; H, 5·3%).

5-Methoxy-1-methylphenanthrene, obtained by heating the preceding acid for 2 hours at 225—230° with quinoline (5 parts) and copper powder (0·5 part), crystallised from methyl alcohol in long hexagonal rods, m. p. 76—77° (Found: C, 86·3; H, 6·25. $C_{16}H_{14}O$ requires C, 86·5; H, 6·3%). The *picrate* separated from alcohol in brick-red needles, m. p. 180—181° (Found: C, 58·5; H, 3·6; N, 9·5. $C_{16}H_{14}O,C_6H_3O_7N_3$ requires C, 58·6; H, 3·8; N, 9·3%).

We are indebted to the Chemical Society for a grant and to Imperial Chemical Industries, Ltd. (Dyestuffs Group), for various gifts of chemicals. We are grateful to Dr. D. W. Adamson for a supply of standard diazomethane solution.

THE COLLEGE OF TECHNOLOGY, MANCHESTER. [*Received, April 24th*, 1937.]

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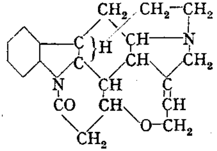
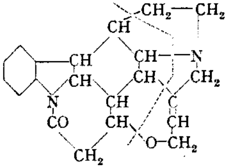
192. *Strychnine and Brucine. Part XXXVI. Preliminary Synthetical Experiments.*

By H. T. OPENSHAW and ROBERT ROBINSON.

THE interpretation of the properties and transformations of strychnine advanced in this series of papers is represented by the expression (I) and it has been repeatedly pointed out



(I) (*a* and *b*).



(II.)

that no clear evidence is available as to which of the alternatives should be preferred.* The slight modification (II) later advocated by Leuchs was the first formula of this type

* Apart from the degradation to carbazole (at relatively high temperatures) the evidence does not exclude a third formula, namely (I*b*), in which the methylene group of the carbazole skeleton is brought down from the β- to the α-position in the indole nucleus. The resulting constitution does not of course contain a carbazole skeleton, but such could readily be formed by migration from the α- to the β-position. The advantage gained by this modification is that the β-position of the indole nucleus bears a hydrogen atom and the chief disadvantage is that it does not look right. The structure, however, like (I*a*) and (I*b*), can be set up on the models without strain.

to be considered by us (J., 1932, 2307), but it was rejected chiefly because strychnine and its derivatives do not exhibit the behaviour of dihydroindoles bearing hydrogen atoms in both α- and β-positions.

The experiments described in the present communication confirm us in the view that the hydroindole nucleus of strychnine is blocked by *gem*-substitution in the α- or β-positions, because we have prepared a substance in the molecule of which methylene replaces carbonyl (that is, it is analogous to strychnidine) and the groups to the right of the dotted line in (II) are replaced by hydrogen atoms; unlike strychnidine, this base may be dehydrogenated with ease and with formation of an aromatic indole derivative.

Before discussing the details of these experiments the opportunity may be taken to reply to the criticisms of M. Kotake (*Proc. Imp. Acad. Tokyo*, 1936, **12**, 99) which are based on the interesting discovery, independently made by Clemo (J., 1936, 1695), that strychninolone, strychninonic acid, or strychnine yields β-indolylethylamine (tryptamine) on fusion with potassium hydroxide. So far from affording material for reasonable doubt of the validity of the structures (I*a*; bridge to the α-position), (I*b*; bridge to the β-position), and (II) it would appear that these observations can be accommodated by any of the three constitutions; the tryptamine skeleton occurs in them all.* The explanation of the degradation of (II) to tryptamine offers the greatest difficulty, but (I*b*) can yield the base by a series of fissions all of which are in accord with analogy. They involve only rupture of C·N links or detachment of substituents from the indole nucleus and both types of reaction are known. The formation of tryptamine from (I*a*) might be the result of migration or of straightforward degradation.

The facts that strychninolone gives the best yield of tryptamine (17%) and methylstrychnine gives none at all (Kotake, Mori, and Mitsuwa, *Sci. Papers Inst. Phys. Chem. Res. Tokyo*, 1937, **31**, 129) will doubtless be eventually significant, but at the moment cannot be brought to bear on the structural problem. In terms of *any* strychnine formula the latter observation shows that the course of the degradation of the molecule is profoundly modified when N-b is alkylated, but there is nothing surprising in this and there is no relevance to the discussion of the merits or demerits of (I*a*) or (I*b*). It is easy, especially on the basis of (I*a*), to devise a plausible explanation of the failure of methylstrychnine to yield tryptamine on fusion with alkali, but such speculations cannot be pursued with much profit.

The new partial structures actually put forward by Kotake are quite unacceptable, not for any abstruse reason but because they fail to take account of some of the most clearly established features of the chemistry of the alkaloids. It is, for example, unnecessary to elaborate the insuperable objections to Kotake's view that the functions of N(a) and N(b), as shown in (I) and (II), should be transposed and that the salt-forming nitrogen atom of strychnine is directly attached to the aromatic nucleus.

The object of the present experiments is to approach the strychnine skeleton as closely as may be in the hope that some degradation product may be synthesised. We have not yet developed a method for the preparation of derivatives of hexahydrocarbazole analogous to (I*a*), but a beginning has been made in the synthesis of a part of the skeleton of (I*b*). Proceeding a few stages further along the lines laid down by Leuchs in his brilliant researches, it should be possible to convert strychninonic acid into the base (III), which is here formulated on the assumption that (I*b*) is the constitution of strychnine, and the synthesis of such a base is our objective.

The action of boiling dilute sulphuric acid on the phenylhydrazone of *cyclo*hexanone-2-β-propionic acid resulted in both indole and indolenine ring closure; the products were the

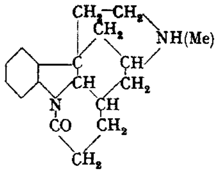
* In connection with Kotake's criticism of our formulations based on the isolation of tryptamine from strychnine, the following quotations from earlier parts of this series are not without interest.

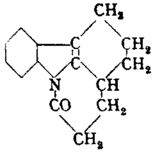
J., 1932, 2308.—" The particular development of the idea adopted in formula (II) was selected (i) because it gives a tryptophan nucleus and beyond this a continuous block of carbon atoms, and (ii) because the arrangement is strainless." Formula (II) is (I*b*).

J., 1934, 1491.—Referring to a formula proposed by Kotake and Mitsuwa—" Although the argument will not have universal appeal, some chemists, including the writer, would reject the formula on the sole ground that it does not contain the tryptophan skeleton."

lactam **of** ***tetrahydrocarbazole*****-1-β-*****propionic acid*** (IV) and ***tetrahydrocarbazolenine*****-11-β-*****propionic acid*** (V).

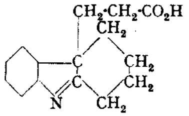
(III.)

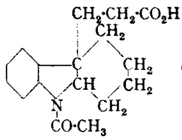




(IV.)

(V.)

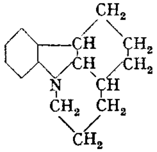


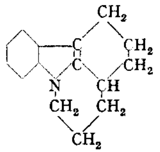


(VI.)

On reduction and acetylation, (V) afforded an *acid* (VI), which exhibited a characteristic Otto reaction. Attempts to reduce the double bond alone in (IV) were unsuccessful, but on electrolytic reduction the *base* (VII) was obtained.

(VII.)



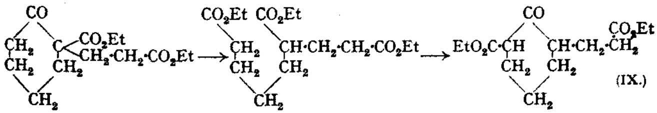


(VIII.)

This *trimethylenehexahydrocarbazole* gives strong strychnidine-type reactions and is readily dehydrogenated on heating with palladised charcoal with formation of *trimethylenetetrahydrocarbazole* (VIII). This substance shows no colour reactions like those of strychnine or strychnidine, but resembles tetrahydrocarbazole in its behaviour.

In order to combine the structural features of (VI) and (VII), we required cyclo*hexanone*-2 : 6-ββ'-*dipropionic acid* and the preparation of this substance proved difficult. Ultimately an excellent method was discovered and this is dependent on a molecular rearrangement which is probably general. The process should be applicable to the synthesis of a variety of 2 : 6-disubstituted *cyclo*hexanones.

Ethyl 2-carbethoxy*cyclo*hexanone-2-β-propionate is transformed by boiling alcoholic sodium ethoxide into *ethyl 6-carbethoxy*cyclo*hexanone*-2-β-*propionate* (IX), the mechanism being obviously alcoholysis and ring-closure in a new position as shown below :

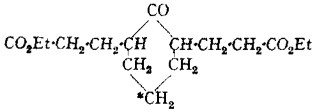


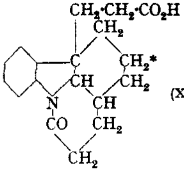
(IX.)

A second propionic acid residue could then be introduced in the usual manner and after hydrolysis and esterification the *ethyl* ester (X) of the required acid was obtained.

The product of the action of alcoholic hydrogen chloride on the phenylhydrazone of (X)

could not be purified, but, after reduction, the ***lactam*** of ***hexahydrocarbazole*-1 : 11-ββ'-*dipropionic acid*** (XI) was isolated. This substance exhibits an Otto reaction.

(X.) 

 (XI.)

We are now attempting to introduce a carboxyl group at the positions denoted by asterisks in (X) and (XI), and if this proves to be possible the final stages in the synthesis of (III) will be a double Curtius reaction and a pentamethylenediamine-piperidine ring closure.

Experimental.

*Ethyl 2-Carbethoxy*cyclo*hexanone-2-β-propionate.*—R. D. Haworth (J., 1933, 1012) obtained this ester (b. p. 199—202°/15 mm.) in 60% yield, and the following conditions have effected some improvement. A solution of sodium ethoxide (from 10 g. of sodium) in alcohol (250 c.c.) was slowly added with shaking to a mixture of ethyl *cyclo*hexanone-2-carboxylate (75 g.), ethyl β-chloropropionate (60 g.), absolute alcohol (150 c.c.), and sodium iodide (1 g.), with cooling in a bath of cold water. The reaction was allowed to proceed at room temperature for 2 hours, and after refluxing for a further 2 hours the greater part of the alcohol was evaporated. The residue was poured into ice-water (2000 c.c.), and the precipitated oil isolated by means of ether. On distillation ethyl carbethoxy*cyclo*hexanonepropionate was collected at 184—185°/13 mm. as an almost colourless oil, giving a negative ferric reaction (yield, 95 g. or 80%) (Found: C, 62·2; H, 8·2. Calc for $C_{14}H_{22}O_5$: C, 62·2; H, 8·1%).

cyclo*Hexanone-2-β-propionic Acid.*—The foregoing ester (10 g.) was hydrolysed by refluxing with concentrated hydrochloric acid (60 c.c.). Solution was complete after 2—3 hours, and after boiling a further hour, the liquid was concentrated to a small bulk under reduced pressure, and diluted with saturated ammonium sulphate solution; an oil then separated, which was collected by means of ether. The extract was dried and evaporated; the residual oil crystallised, on cooling, in minute colourless prisms (5·8 g. or 90%). A sample recrystallised from light petroleum (b. p. 40—60°) had the recorded m. p. 55°.

Haworth (*loc. cit.*) carried out this hydrolysis with methyl-alcoholic potassium hydroxide, and obtained the acid, together with the anhydride of heptane-1 : 3 : 7-tricarboxylic acid.

The Condensation of cyclo*Hexanone-2-β-propionic Acid with Phenylhydrazine.*—A mixture of the keto-acid (27·5 g.) and phenylhydrazine (17·5 g.) was gently heated until reaction commenced; the oily phenylhydrazone was then formed with liberation of heat. The product was treated with boiling dilute sulphuric acid (300 c.c. of 20%) for 10 minutes with shaking; the brownish oil thus obtained crystallised on cooling. It was collected, washed with water, and recrystallised from alcohol. The ***lactam*** of ***tetrahydrocarbazole*-1-β-*propionic acid*** (IV) separated in hexagonal plates with a faint bluish tinge, m. p. 121° (20 g.). Two further crystallisations from alcohol or glacial acetic acid raised the m. p. to 126° (Found: C, 80·0; H, 6·7; N, 6·3. $C_{15}H_{15}ON$ requires C, 80·0; H, 6·7; N, 6·2%).

The aqueous filtrate from the reaction mixture was washed twice with ether, made weakly alkaline with dilute aqueous ammonia, and neutralised with acetic acid; the liquid became turbid, and on stirring deposited a pale yellow, crystalline solid (9 g.). On recrystallisation from a moderately large volume of alcohol, ***tetrahydrocarbazolenine*-11-β-*propionic acid*** separated in nearly colourless prisms, m. p. 226°. For analysis, the substance was crystallised twice more from alcohol without raising the m. p. (Found: C, 74·3; H, 6·9. $C_{15}H_{17}O_2N$ requires C, 74·1; H, 7·0%). The compound is insoluble in water, ether and benzene; it dissolves readily in dilute acids or alkalis.

Reduction of the Lactam of Tetrahydrocarbazole-1-β-propionic Acid.—Attempts to reduce this substance with hydrogen and platinum, with tin and aqueous-alcoholic hydrochloric acid, and with sodium and ethyl or *iso*amyl alcohol were unsuccessful; it was readily reduced electrolytically at a lead cathode.

The lactam (10 g.) was dissolved in warm glacial acetic acid (300 c.c.), and the solution was diluted with 15% sulphuric acid (100 c.c.) and placed in the cathode chamber of the usual apparatus. A current of 5 ampères was passed for 24 hours; the liquid, which was stirred occasionally, maintained itself at 40°. The colourless solution was filtered, diluted with water, and mixed with dilute aqueous potassium hydroxide. A white crystalline solid was precipitated before the liquid had become alkaline, and this was collected, washed with water, and dried (10 g.). The compound was freely soluble in cold light petroleum, benzene or ethyl acetate. It was crystallised from a little hot acetic acid, 1 : 9-*trimethylenehexahydrocarbazole* (VII) being obtained in lozenge-shaped, glistening, colourless plates, m. p. 81—82°. For analysis, a specimen was crystallised from methyl alcohol; the m. p. was unchanged (Found : C, 84·6; H, 8·7; N, 6·7. $C_{15}H_{19}N$ requires C, 84·5; H, 8·9; N, 6·6%). This base is readily soluble in 5% hydrochloric acid, and on the addition of a trace of ferric chloride, an intense red coloration which is stable for several hours is produced.

Dehydrogenation of 1 : 9-*Trimethylenehexahydrocarbazole*.—(A) The substance (1 g.) was dissolved in glacial acetic acid (15 c.c.), cooled to room temperature, and mixed with a solution of mercuric acetate (6 g.) in 10% aqueous acetic acid (15 c.c.). The heterogeneous mixture, kept at room temperature, at first developed a bright red colour, but after 24 hours this had changed to a yellowish-brown, and the bulk of the insoluble matter had increased considerably. The solid was collected, washed with 50% acetic acid, and pressed as dry as possible (7 g.). The slightly sticky solid thus obtained was suspended in a hot mixture of 50% acetic acid (20 c.c.) and acetone (30 c.c.), saturated with hydrogen sulphide, and filtered hot from the mercury sulphide, which was washed with hot acetone. The filtrate and washings were combined and evaporated until a turbidity appeared; on cooling, a sticky solid (occasionally an oil) separated. This was isolated, washed with dilute acetic acid, then with water, and dissolved in concentrated hydrochloric acid. The filtered solution was diluted with twice its volume of water; a brownish solid then separated. This was collected and washed with dilute hydrochloric acid. It was crystallised from methyl alcohol (norit), pale yellow, lozenge-shaped leaflets of 1 : 9-*trimethylene*-1 : 2 : 3 : 4-*tetrahydrocarbazole*, m. p. 85—86°, being obtained (0·1 g.). Further crystallisation raised the m. p. to 86—87°. The compound was insoluble in dilute hydrochloric acid, and gave no colour with ferric chloride and dilute acid. A mixture with trimethylenehexahydrocarbazole melted at 68—71°. Basification of the last acid filtrate afforded 0·2—0·3 g. of the initial material. The following process is the more convenient and gives a better yield.

(B) Trimethylenehexahydrocarbazole (0·8 g.) was heated at 170—195° with palladised charcoal (prepared according to Ruzicka) for 7½ hours; hydrogen (63 c.c.; theoretical, 90 c.c.) was slowly evolved. After cooling, the product was dissolved in warm concentrated hydrochloric acid (7 c.c.) and filtered from the catalyst. The yellow solution was diluted with 2—3 times its volume of water, a white crystalline precipitate being formed. After stirring and standing for a short time, the 1 : 9-trimethylenetetrahydrocarbazole was collected, washed with dilute hydrochloric acid, then with water, and dried (0·5 g.). It was recrystallised from methyl alcohol, yielding almost colourless leaflets, m. p. 87—88°, not raised by further recrystallisation (Found : C, 85·1; H, 8·2; N, 6·7. $C_{15}H_{17}N$ requires C, 85·3; H, 8·1; N, 6·6%). When the acid filtrate was made alkaline, a quantity of the initial material was recovered.

With Ehrlich's reagent on boiling, a bluish-green coloration is produced. This fades to yellow on cooling and the changes may be repeated as often as desired. This behaviour is similar to that of other 2 : 3-substituted indoles.

N-*Acetylhexahydrocarbazole*-11-β-*propionic Acid* (VI).—A mixture of tetrahydrocarbazolenine-11-β-propionic acid (4 g.), concentrated hydrochloric acid (10 c.c.), and granulated tin (4 g.) was refluxed for 8 hours; on dilution of the hot filtered solution a colourless gum separated. This was detinned in aqueous suspension in the usual way, and the filtrate boiled to expel hydrogen sulphide, cooled, and neutralised by means of ammonia and acetic acid. The gum that separated could not be crystallised; it was mixed with acetic anhydride (15 c.c.), and the solution refluxed for 5 hours. On keeping, the product obtained after decomposition of the acetic anhydride with water crystallised and the *substance* separated from alcohol in colourless prisms, m. p. 202° (Found : C, 71·1; H, 7·4. $C_{17}H_{21}O_3N$ requires C, 71·1; H, 7·3%). A suspension of the substance in 60% sulphuric acid gave an intense reddish-purple coloration on the addition of a trace of potassium dichromate; the colour rapidly faded through red to brownish-yellow.

*Ethyl 6-Carbethoxy*cyclo*hexanone-2-β-propionate* (IX).—A mixture of ethyl 2-carbethoxy*cyclo*hexanone-2-β-propionate (52 g.) and alcoholic sodium ethoxide (70 c.c.; 4·8 g. of sodium) was refluxed for 8 hours. The ester was then isolated in the usual manner and distilled, b. p. 189—192°/11 mm. (30·6 g.). The fraction, b. p. 120—188°/11 mm., gave a further 6·2 g. on redistilla-

tion, making the yield 70%. The *product* distilled again at 189—190°/11 mm. (Found: C, 62·3; H, 8·3. $C_{14}H_{22}O_4$ requires C, 62·2; H, 8·1%). The ferric reaction in alcoholic solution was a deep violet coloration.

Ethyl 6-*Carbethoxy*cyclo*hexanone*-2 : 6-ββ'-*dipropionate*.—The foregoing keto-ester (36·8 g.) was added to a suspension of sodium powder (3·1 g.) in benzene (80 c.c.); the solution of the sodium was completed by refluxing for 2 hours. The orange liquid was cooled, and ethyl β-chloropropionate (18·5 g.) introduced. As there was no sign of immediate reaction, the mixture was refluxed for 5 hours; no solid, however, was precipitated from the slightly turbid solution. The reaction product was mixed with water and a few drops of hydrochloric acid and the ester was isolated by means of ether and distilled, b. p. 195—197°/0·4 mm. (yield, 38·1 g. or 75%). A sample was redistilled, b. p. 182—183°/0·2 mm. (Found: C, 61·3; H, 8·1. $C_{19}H_{30}O_7$ requires C, 61·6; H, 8·1%). The condensation in alcoholic solution gave a poor yield of the desired *product*, and a considerable quantity of *ethyl heptane*-1 : 3 : 7-*tricarboxylate*, b. p. 147—148°/0·15 mm., was formed as the result of alcoholysis (Found: C, 61·0; H, 8·8. $C_{18}H_{28}O_6$ requires C, 60·8; H, 8·9%). When this ester was treated with sodium in benzene with a trace of alcohol, and subsequently with ethyl β-chloropropionate, an 80% yield of ethyl carbethoxy*cyclo*hexanonedipropionate was obtained.

cyclo*Hexanone*-2 : 6-ββ'-*dipropionic Acid and its Ethyl Ester* (X).—A mixture of ethyl carbethoxy*cyclo*hexanonedipropionate (38 g.) and concentrated hydrochloric acid (250 c.c.) was refluxed for 30 minutes and the clear solution was then evaporated to dryness, finally under diminished pressure. The residue crystallised (24·5 g. or 98%) and the solid was collected, washed with saturated aqueous ammonium sulphate and then with a little water, and dried at 100°. Crystallisation from ethyl acetate afforded colourless prisms (14·5 g.), m. p. 145° (Found: C, 59·4; H, 7·4. $C_{12}H_{18}O_5$ requires C, 59·5; H, 7·4%), and the gummy acid in the mother-liquor was set aside for combination with another batch and for recovery by esterification.

The crystallised acid (14·5 g.) was treated in an automatic separation apparatus ("Organic Syntheses," Coll. Vol. I, 256) with alcohol (10 c.c.), carbon tetrachloride (30 c.c.), and two drops of concentrated sulphuric acid; separation of water ceased after an hour. The *ester* was isolated in the usual way and crystallised on cooling (17 g. or 95%). It separated from light petroleum in colourless prisms, m. p. 60—61° (Found: C, 64·5; H, 8·8. $C_{16}H_{26}O_5$ requires C, 64·4; H, 8·7%).

The Lactam of Hexahydrocarbazole-1 : 11-ββ'-*dipropionic Acid* (XI).—The foregoing ester (5 g.) and phenylhydrazine (1·8 g.) were melted together, a few drops of glacial acetic acid added, and the mixture kept for ½ hour at 60—70°. Reaction occurred with separation of water. The oily phenylhydrazone was taken up in ether, washed with water, dried with potassium carbonate, and recovered as an orange-coloured oil which could not be crystallised.

This phenylhydrazone was dissolved in alcohol (10 c.c.), and the solution was saturated with dry hydrogen chloride at first with cooling in ice, but after 5 minutes the bath was removed and the mixture then heated itself to about 70°. A precipitate of ammonium chloride was rapidly formed. The mixture was allowed to cool, concentrated hydrochloric acid (25 c.c.) and tin (5 g.) added, and the whole gently boiled in an open flask so that the alcohol might be evaporated. After an hour, the boiling was continued under reflux for a further 4 hours; the tin had then almost completely disappeared. The cooled solution was diluted with water (75 c.c.); the colourless oil then precipitated became crystalline on stirring and keeping. It was collected, washed with water, and treated with warm aqueous sodium carbonate. The solution was filtered and on acidification yielded a white solid (0·5 g.). This was dried at 100°, dissolved in a small quantity of hot glacial acetic acid, and diluted with an equal volume of water. On cooling, the *lactam* of *hexahydrocarbazole*-1 : 11-ββ'-*dipropionic acid* separated in colourless, elongated prisms, m. p. 269—270°. Recrystallisation from 50% aqueous acetic acid raised the m. p. to 271°, with previous sintering (Found: C, 72·1; H, 7·0; N, 4·7. $C_{18}H_{21}O_3N$ requires C, 72·2; H, 7·0; N, 4·7%).

A solution of the substance in 60% sulphuric acid gave a transient deep purple coloration on the addition of a trace of aqueous potassium dichromate. The colour faded through rose-red to yellow and was inherently unstable, because the addition of more dichromate to the yellow solution gave again a purple coloration.

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Dyson Perrins Laboratory, Oxford University. [*Received, May 6th, 1937.*]

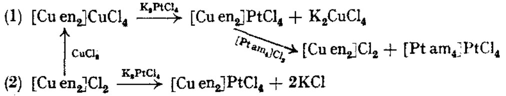
193. *The Chelation of Diamines with Cupric Salts.*

By F. W. Chattaway and H. D. K. Drew.

Cupric chloride reacts with ethylenediamine to give three substances, to which the formulæ Cu $enCl_2$, Cu en_2Cl_2, and Cu en_3Cl_2 have been given (see, *e.g.*, Dubsky and Dostál, *Pub. Fac. Sci. Univ. Masaryk*, 1932, No. 160, 3). Cupric sulphate behaves similarly (Grossmann and Schück, *Z. anorg. Chem.*, 1906, **50**, 16). The salts of the third type are relatively unstable, readily changing into those of the second type by the loss of a molecule of diamine. With a view to study the stereochemistry of copper, we re-examined the action of cupric chloride with ethylenediamine and extended the work to the case of *iso*butylenediamine (ib). The point of chief interest which arose was that the supposed Cu $enCl_2$ is in reality a dimeric substance, *bisethylenediaminocupric cuprichloride*, [Cu en_2]$CuCl_4$, and that the *isobutylenediamino*-analogue also has this structure. They are greenish-blue, like hydrated cupric chloride, contrasting with the purple Cu en_2Cl_2 and Cu ib_2Cl_2; in aqueous solution their ions are in equilibrium with those of Cu en_2Cl_2 (or of Cu ib_2Cl_2) and of cupric chloride, as can be inferred from the fact that the cuprichlorides separate satisfactorily from saturated aqueous solutions only when an excess of cupric chloride is added.

It has frequently been suggested that the saturated solutions of simple copper salts contain anions such as $CuCl_4''$. In particular, Kohlschütter (*Ber.*, 1904, **37**, 1161) demonstrated experimentally that this anion was discharged at the anode during the electrolysis of solutions containing cupric chloride, and he also postulated the presence of the kation $Cu(H_2O)_4^{\cdot\cdot}$. Our observations are in agreement with this suggestion in so far as the formal analogy between the structures [Cu en_2]$CuCl_4$ and [$Cu(H_2O)_4$]$CuCl_4$ may be regarded as relevant. This consideration led us to examine the case of copper sulphate and we found here also that the substance formulated by Grossmann and Schück (*loc. cit.*) as Cu $enSO_4,3H_2O$ was really the dimeric *cuprisulphate hexahydrate*, [Cu en_2][$Cu(SO_4)_2,6H_2O$]. Since the kation is the same as that in the cuprichloride, it is presumably anhydrous, and since the copper of the anion is electronically saturated, the six water molecules must be associated with the sulphate radicals. If, therefore, copper sulphate pentahydrate can be regarded as a cuprisulphate, it must have the formula [$Cu(H_2O)_4$][$Cu(SO_4)_2,6H_2O$], in which again six water molecules are associated with the sulphate radicals. The analogy is remarkable when taken in conjunction with that of the chlorides. On the contrary, Beevers and Lipson, as the result of an *X*-ray study (*Proc. Roy. Soc.*, 1934, *A*, **146**, 570), have deduced that in $CuSO_4,5H_2O$ each copper atom is surrounded by four water molecules, the fifth being united to two other water molecules and to two sulphate oxygen atoms.

The dimeric character of the foregoing co-ordinated salts was proved by the following reactions (shown for the compounds of en only, but carried out also with those of ib):



Thus the two compounds which Dubsky and Dostál formulated as Cu $enCl_2$ and Cu en_2Cl_2 give, on treatment with potassium chloroplatinite, the same plato-salt, half the copper being eliminated in the case of the first substance.

With dilute hydrochloric acid, even in the cold, [Cu en_2]$CuCl_4$ gives the yellow salt [en H_2]$CuCl_4$, described by Grossmann (*Z. anorg. Chem.*, 1906, **50**, 1); this reaction was reversed by aqueous sodium hydroxide. It was not found possible to isolate an intermediate stage in which the chelate loops are opened but not detached from copper, as was effected in the case of the platinum analogue (Drew and Tress, J., 1933, 1335). Copper is bound much less firmly to the chelating diamines than is platinum (cobalt is intermediate); we were unable to isolate geometric isomerides of Cu ib_2Cl_2 or to resolve it as the *α-bromocamphor-π-sulphonate.*

EXPERIMENTAL.

Bisethylenediaminocupric cuprichloride, [Cu en_2]$CuCl_4$, was prepared from an aqueous solution of hydrated cupric chloride (5·3 g.) and ethylenediamine (1·9 g.). It formed light greenish-blue needles, m. p. 233° (Found: C, 12·15; H, 4·2; N, 14·05. $C_4H_{16}N_4Cl_4Cu_2$ requires C, 12·3; H, 4·1; N, 14·4%); it dissolved readily in water but not in organic solvents. If twice the amount of ethylenediamine was used, bisethylenediaminocupric chloride was formed; it was extracted with cold ethyl alcohol and then crystallised from this solvent several times, forming deep purple needles of the monohydrate, m. p. 218° (Found: N, 20·7; H_2O, 6·55. Calc. for $C_4H_{16}N_4Cl_2Cu,H_2O$: N, 20·55; H_2O, 6·6%).

The corresponding chloroplatinite, [Cu en_2]$PtCl_4$, was prepared from either of the above salts and aqueous potassium chloroplatinite. It formed lilac-pink crystals nearly insoluble in water (Found: C, 9·35; H, 3·3; N, 10·7. Calc. for $C_4H_{16}N_4Cl_4CuPt$: C, 9·2; H, 3·1; N, 10·75%). Grünberg (*Z. anorg. Chem.*, 1926, **157**, 173) described this salt as a violet-red substance obtained on heating the salt [Cu en_3]$PtCl_4$ or allowing it to stand.

[en H_2]$CuCl_4$, prepared by adding dilute hydrochloric acid (2 or 4 equivs.) to aqueous [Cu en_2]$CuCl_4$, formed golden-yellow leaflets, m. p. 272° (Found: C, 9·0; H, 3·9; N, 10·9; Cl, 52·0; Cu, 24·0. Calc.: C, 9·0; H, 3·75; N, 10·5; Cl, 53·1; Cu, 23·8%). The same compound was produced from [Cu en_2]Cl_2 and hydrochloric acid.

Bisisobutylenediaminocupric cuprichloride, [Cu ib_2]$CuCl_4$, from cupric chloride and *iso*butylenediamine *or* from [Cu ib_2]Cl_2 and aqueous cupric chloride, formed light blue or bluish-green plates, m. p. 232° (decomp.), soluble in water or hot alcohol (Found: C, 21·3, 21·4; H, 5·6, 5·9; N, 12·3; Cu, 28·4. $C_8H_{24}N_4Cl_4Cu_2$ requires C, 21·55; H, 5·4; N, 12·6; Cu, 28·6%). The corresponding *chloride*, obtained as for the ethylenediamino-analogue, formed dark-purple crystals, very soluble in water and soluble in cold alcohol; the air-dried substance melted at 245° (frothing) and appeared to be a hemihydrate (Found: C, 29·5; H, 8·25; H_2O, 2·7, 2·9. $C_8H_{24}N_4Cl_2Cu,\frac{1}{2}H_2O$ requires C, 30·0; H, 7·8; H_2O, 2·8%), but a *dihydrate* was also obtained (Found: N, 16·1, 16·3; Cu, 18·3. $C_8H_{24}N_4Cl_2Cu,2H_2O$ requires N, 16·15, Cu, 18·3%). The *chloroplatinite* formed lilac crystals, m. p. about 228° (decomp.), insoluble in water (Found: C, 16·7; H, 4·5; N, 10·0. $C_8H_{24}N_4Cl_4CuPt$ requires C, 16·65; H, 4·2; N, 9·7%). The chloropalladite was unstable, decomposing in contact with the aqueous reaction solution into a soluble copper salt and *isobutylenediaminopalladous chloride*, which formed dark yellow, domed prisms, recrystallisable from water (Found: Pd, 40·6. $C_4H_{12}N_2Cl_2Pd$ requires Pd, 40·2%).

Bisisobutylenediaminocupric α-bromocamphor-π-sulphonate was obtained from the chloride and ammonium α-bromocamphor-π-sulphonate in aqueous solution, as mauve reactangular plates, m. p. 237°, readily crystallised from water (Found: Cu, 7·3. $C_{28}H_{52}O_8N_4Br_2S_2Cu$ requires Cu, 7·4%).

Bisethylenediaminocupric cuprisulphate hexahydrate formed light blue crystals, which were drained on porous tile and air-dried (Found: Cu, 23·6; H_2O, 19·55. $C_4H_{16}N_4O_8S_2Cu_2,6H_2O$ requires Cu, 23·2; H_2O, 19·75%). With potassium chloroplatinite it gave [Cu en_2]$PtCl_4$, half the copper being set free as copper sulphate.

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194. *Addition of Hydrogen Bromide to Non-terminal Double Bonds. Effect of the Alkyl Groups.*

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PRELIMINARY experiments (Harris and Smith, J., 1935, 1108) showed that the product of the action of hydrogen bromide on *iso*undecenoic acid [$CH_3·CH:CH·(CH_2)_7·CO_2H$] contained approximately 57% of 9-bromoundecoic acid and that the true percentage would probably be lower.

This result was more in harmony with that of Lauer and Stodola (*J. Amer. Chem. Soc.*, 1934, **56**, 1215), who found 53% of 3-bromopentane in the product of the addition of hydrogen bromide to Δ^2-pentene, than with the results of Lucas and Moyse (*ibid.*, 1925, **47**, 1459) and Kharasch and Darkis (*Chem. Reviews*, 1928, **5**, 590), who found 79% of 3-bromopentane.

By the synthesis of 9-bromoundecoic acid and use of the binary system with 10-bromoundecoic acid it has been possible to make a more accurate analysis of the products from *iso*undecenoic acid. The reaction in hexane solution was very slow and also in acetic acid (considering the high solubility of hydrogen bromide in acetic acid), but the figures given in Table I show that the analyses steadily approach 50% of the 10-bromo-acid as the olefin is eliminated.

A further attempt (compare Harris and Smith, *loc. cit.*) to detect a "peroxide" effect by carrying out simultaneously an experiment in which strongly "oxidant" conditions prevailed and a second with rigorously "antioxidant" conditions showed that the variation in composition of the products was within the margin of error. Kharasch and McNab (*Chem. and Ind.*, 1935, **13**, 990) similarly failed to detect a "peroxide" effect with non-terminal double bonds. If the "abnormal or peroxide catalysed reaction" is one which involves a reversal of orientation of addition, the reversal would scarcely be detected when the "normal" reaction gave the isomerides in the proportion 50 : 50 or 51 : 49. (With *terminal* double bonds a "normal" reaction yielding 90% of $CH_3{\cdot}CHBr{\cdot}[CH_2]_n{\cdot}$ is replaced by a more rapid "abnormal" reaction yielding 90% of $CH_2Br{\cdot}CH_2{\cdot}[CH_2]_n{\cdot}$.) It is possible that the high rate of the reaction in benzene despite the low concentration of hydrogen bromide is connected with the fact that benzene is a solvent which favours the "abnormal" reaction (compare Ashton and Smith, J., 1934, 437).

At the time when the addition products of *iso*undecenoic acid were thought to contain approximately 43% of the 10-bromo-acid it was represented to us that the proportion of 10-bromo-acid had been raised by the influence of the terminal carboxyl group, and that our assumption of the equivalence of $\cdot[CH_2]_7{\cdot}CO_2H$ and $\cdot[CH_2]_7{\cdot}CH_3$ was unjustified. As the difficulties of carrying out a similar investigation with an olefin $CH_3{\cdot}CH{:}CH{\cdot}[CH_2]_n{\cdot}CH_3$ were insuperable, it was decided to alter the end group of *iso*undecenoic acid in two ways. A change of carboxyl to amido was not expected to have any appreciable effect on the composition of the addition product, but the amide as a high-melting solid would give valuable confirmation of the results from the acid. The slightly lower percentages of 10-bromo-acid observed (46% and 47%) were due to impurities introduced by the extra processes involved.

Reduction of the carboxylic acid to the alcohol and addition of hydrogen bromide to the latter would be a severer test, since in the alcohol there should be no opposition by the end group to any general effect in the alkyl chain :

Oxidation of the mixture of bromo-alcohols gave the bromo-acids slightly contaminated with by-products which were not removed by fractional distillation. The melting points from the binary system show that the mixtures must contain at least 44% of the 10-bromo-acid, and on the assumption that the impurities have molecular weights of 100—300, the ratio of the bromo-acids must be very near to 50 : 50; the same ratio should hold for the bromo-alcohols before oxidation.

In *iso*undecenoic acid, therefore, the observed composition of the addition product is not the combined result of a tendency of the alkyl chain to produce excess of 9-bromo-acid and of an opposite tendency of the carboxyl group exactly balanced. (If the carboxyl group had any influence, this should vary greatly in such different solvents as hexane and acetic acid. A better test for the transmission of the influence of end groups through a chain or a solvent would be an investigation of the nuclear reactions of quinol ethers $MeO{\cdot}C_6H_4{\cdot}O{\cdot}[CH_2]_n{\cdot}CO_2H$; compare Robinson and Smith, J., 1926, 392; Bradfield and Jones, J., 1928, 1011.)

Although it would not be justifiable to assume the equivalence of carbon atoms 9 and 10 of *iso*undecenoic acid in other circumstances, yet in the particular reaction studied—the addition of hydrogen bromide in solvents of widely different nature—these carbon atoms appear to be equally activated, just as do carbon atoms 2 and 3 in Δ^2-pentene (Lauer and Stodola, *loc. cit.*). It would appear, therefore, that in a homologous series,

CH_3·CH:CHR, there is no appreciable change in the relative activity of the unsaturated carbon atoms. It is of interest to compare this result with those of measurements of reactivity in other homologous series, and the following classification has been found to group the most carefully studied series into only three types. In the majority of reactions there is a great *decrease* in reactivity in passing from the first member (1 CH_2 group) to the third member and then a slower decrease along the series: Type I of Homologous Series Reactivity. Examples are the reactions of *n*-alkyl halides with trimethylamine, sodium methoxide or sodium benzyloxide; the hydrolysis of esters and the esterification of alcohols (for bibliography, see Haywood, J., 1922, **121**, 1904; Moelwyn-Hughes, *Chem. Reviews*, 1932, **10**, 263).

When some unsaturated group or atom is present, large *alternations* in reactivity for the first three or four members are shown, followed by a gradual decrease in reactivity (Type II). Examples are the reactions between CH_3·CO·O·$[CH_2]_n$·Cl or CH_3·CO·$[CH_2]_n$·Cl and potassium iodide (Conant, Kirner, and Hussey, *J. Amer. Chem. Soc.*, 1925, **47**, 488); Ph·S·$[CH_2]_n$·OH and hydrogen bromide (Bennett and Mosses, J., 1931, 2956); the hydrolysis of aliphatic amides (Crocker, J., 1907, **91**, 593); and possibly the dissociation constants of *n*-aliphatic acids.

In a few reactions there is an *increase* of reactivity with increase in length of the carbon chain (Type III). Examples are the relative directive powers of alkoxy-groups as shown by the nitration of *p*-alkoxyanisoles (Robinson and Smith, *loc. cit.*); the rate of chlorination of alkyl ethers of phenol (Bradfield and Jones, *loc. cit.*); and the rate of conversion of alkylamine acetates into amides (Musselius, *J. Russ. Phys. Chem. Soc.*, 1900, **32**, 29). In the reactions of the ethers mentioned above, the results could also be interpreted as showing a *decreasing* effect of a longer alkyl chain on the oxygen atom (Type II).

The addition of hydrogen bromide to a series of olefins with non-terminal double bonds shows a new kind of Homologous Series Reactivity, Type IV: constant reactivity with increasing alkyl chain. Apparently the carbon atoms joined by the double bond are not activated by such a small disturbance as the difference between the general effect of an alkyl chain and that of a methyl group, and the reaction with hydrogen bromide is the result of a collision between a hydrogen bromide molecule and an olefin molecule with sufficient vibrational energy in the double bond.

Isolation of 9-*ketoundecoic acid* from the mixture obtained by hydration of undecynoic acid was achieved by making use of the fact that the 10-keto-acid as a methyl ketone gave a sodium bisulphite addition compound, while the ethyl ketone remained unaffected. The substance isolated by Myddleton and Barrett (*J. Amer. Chem. Soc.*, 1927, **49**, 2258) by a tedious series of crystallisations and thought to be 9-ketoundecoic acid (m. p. 43·5°) was actually the eutectic mixture of the two acids.

9-*Hydroxy*- and 9-*bromo-undecoic acids* had lower melting points than the corresponding 10-substituted compounds, but otherwise were very similar and there was no evidence of conversion of 9- into 10-bromo-acid during the addition reactions.

EXPERIMENTAL.

9- *and* 10-*Ketoundecoic Acids.*—$\Delta^{9:10}$-Undecynoic acid (12 g.), m. p. 60°, added to ice-cold sulphuric acid (150 c.c. of 85%), yielded after 48 hours 11·5 g. of distilled keto-acids, m. p. 44—45° (compare Myddleton and Barrett, *loc. cit.*).

Separation of the Keto-acids.—The keto-acid mixture (20 g.) in benzene (150 c.c.) was shaken with concentrated sodium bisulphite solution (400 c.c.) during 70 hours. The bisulphite compound of the 10-keto-acid, filtered off, washed with benzene, and warmed with dilute hydrochloric acid, yielded 9 g. of keto-acid, m. p. 53—55°; this crystallised from benzene–light petroleum in plates (6 g.), m. p. 59°. The semicarbazone melted at 135—136° (Chuit, Boelsing, Hausser, and Malet, *Helv. Chim. Acta*, 1926, **9**, 1074, give m. p. 134—135°).

9-*Ketoundecoic Acid.*—The filtrate from the sodium bisulphite compound of the 10-keto-acid gave on concentration 10 g. of crystals, m. p. 55—57°. After two crystallisations from light petroleum these melted at 58—59° (plates); yield, 7 g. (Found: C, 65·8; H, 9·9. $C_{11}H_{20}O_3$ requires C, 66·0; H, 10·0%). The *semicarbazone* crystallised from alcohol in prisms, m. p. 161° (Found: N, 16·2. $C_{12}H_{23}O_3N_3$ requires N, 16·3%).

Because of the similarity in the melting points the following mixed m. p.'s were taken:

9-*keto-acid* (m. p. 58—59°) with $\Delta^{9:10}$-undecynoic acid (m. p. 61°) gave a mixed m. p. 43—47°; 9-keto-acid with 10-keto-acid, mixed m. p. 43—45°; 10-keto-acid with undecynoic acid, 43—47°.

9-*Hydroxyundecoic Acid.*—Reduction of the 9-keto-acid in alcoholic solution with sodium amalgam (2—4%) was slow, and amalgam from highly purified mercury was almost without action on the ketone. Reduction of the keto-ester with *iso*propyl alcohol and aluminium *iso*propoxide (Ponndorf, *Z. angew. Chem.*, 1926, **39**, 138) gave good results. Methyl 9-ketoundecoate (15 g., from the keto-acid and methyl alcohol in presence of sulphuric acid), aluminium *iso*propoxide (10 g.), and *iso*propyl alcohol (200 c.c.) were heated in a flask provided with an efficient fractionating column so that liquid very slowly distilled during 2 hours. After the solvent had been evaporated, some of the hydroxy-ester was extracted with ether, but much was still mixed with the aluminium compounds. Concentrated hydrochloric acid was then added, and superheated steam passed until no more oily drops distilled. The total yield of hydroxy-ester (and hydroxy-acid) was then hydrolysed with alcoholic potassium hydroxide and gave 10·5 g. of crude hydroxy-acid, m. p. 26°. After two crystallisations from benzene–light petroleum the *acid* melted at 34—35° (Found: C, 65·3; H, 10·8. $C_{11}H_{22}O_3$ requires C, 65·3; H, 10·9%).

9-*Bromoundecoic Acid.*—The hydroxy-acid (4 g.) was heated to 130° during 6 hours while a slow stream of dry hydrogen bromide was passed through the liquid. The product was dissolved in ether, and the ethereal solution washed, dried and evaporated. The distilled *bromo-acid* melted at 22°, and after one crystallisation from hexane, at 27°; yield, 3 g. After four similar crystallisations it had a constant m. p. 30·0° (thermometer in the liquid) and m. p. 31° in a capillary tube (Found: C, 49·7; H, 7·9. $C_{11}H_{21}O_2Br$ requires C, 49·8; H, 7·9%).

Mixtures of 9- *and* 10-*Bromoundecoic Acids.*—These all crystallised slowly and the m. p.'s (clearing points) were taken in the Beckmann apparatus. Mixtures containing 45—57% of the 9-bromo-acid showed a decided arrest at —6° to —4° on heating and often melted completely at this point, but stirring at —5° or seeding with the 10-bromo-acid (m. p. 35·7°) produced the higher-melting form. The eutectic point (16·5° from the curves) was rather indefinite.

As was assumed by Harris and Smith, the curve for the depression of m. p. of 10-bromoundecoic acid by the 9-bromo-acid exactly covers the curve for depression by the 11-bromo-acid.

9-Bromo-acid, mols. %	100	88·8	79·4	71·9	66·1	62·7	59·7	57·5	55·25
M. p.	30·0°	26·65°	23·90°	21·45°	19·45°	18·35°	17·3°	16·5°	17·3°
9-Bromo-acid, mols. %	53·2	51·05	48·1	45·3	37·5	26·05	17·9	10·0	0·0
M. p.	18·55°	19·65°	20·75°	22·05°	24·95°	28·75°	31·30°	33·17°	35·68°

$\Delta^{9:10}$-*Undecenoic Acid* (iso*Undecenoic Acid*).—Reduction of the mixture of 9- and 10-iodoundecenoic acids (Harris and Smith, *loc. cit.*) with zinc turnings and propionic acid was complete in 48 hours. The product, m. p. 11—13°, was crystallised to m. p. 19·2° (thermometer in the liquid) and iodine number (Hanuš) 138 (calc., 138). For experiments I to M it was necessary to use the purest *iso*undecenoic acid.

Catalytic reduction of $\Delta^{9:10}$-undecynoic acid (hydrogen with colloidal palladium or with nickel) gave products melting at 0—8° and in each case the m. p. was raised 2—3° by allowing the liquid to stand with nitrous acid. This probably indicated a change of *cis*- into *trans-iso*-undecenoic acid, but, as saturated impurities were always present, purification was so tedious that the catalytic method was abandoned.

Addition of Hydrogen Bromide.—In the addition experiments of Harris and Smith (*loc. cit.*, p. 1110) the products usually contained a trace of olefin, and, as the analyses and determinations of the equivalents showed, this was not eliminated by distillation. In the present experiments the time for complete saturation of the double bond, especially when hexane was used as solvent, was much greater than had been anticipated. With benzene as solvent, completely saturated products were finally obtained, and after distillation without any attempt at fractionation these gave correct analyses; repeated distillation caused no change in m. p. All the products showed a lower m. p. (— 6° to — 4°), but the eutectic arrest (near + 16°) was very indefinite (as with mixtures of the synthetic acids) and could not be used as a criterion of purity. Addition of a known weight of 10-bromoundecoic acid and redetermination of the m. p. showed on which branch of the curve the product lay, and also confirmed the composition given by the original m. p.

Expts. A—H. The products of experiments A—H (Harris and Smith) had been mixed. As the mixture appeared more strongly reducing than would be accounted for by the presence of any of the catalysts used, 5 g. of it were dissolved in acetic acid (50 c.c.), and the solution kept saturated with hydrogen bromide during 9 days. The solution then reduced very dilute permanganate–sodium carbonate solution only after 3 hours. The product, isolated by dilution

with water and extraction with hexane, distilled at 150—157°/0·2 mm. and had *M*, 264, m. p. 19·9° (49·5% of 10-bromoundecoic acid).

In the following experiments hydrogen bromide, not specially dried or freed from air, was passed for 1 hour into a solution (usually 30 c.c.) of pure *iso*undecenoic acid (2 g., m. p. 19·2°) at 0°. The flask was then sealed and kept at room temperature.

Expt. I. Hexane. After 15 hours (50 c.c. of hexane being used instead of 30 c.c.) the solution still reduced permanganate and the product had m. p. approx. 17°. After having stood 50 hours, the hexane solution on evaporation gave 2·64 g. (92% yield) of bromo-acids, *M*, 262 (calc., 265) and m. p. 18·3° (46·2% of 10-bromo-acid). Confirmation: 0·5307 g. of product I, mixed with 0·4142 g. of 10-bromoundecoic acid, had m. p. 27·6°, whence 70·0% yield of 10-bromo-acid in the mixture and 46·6% in product I. The remainder of I was treated with hydrogen bromide in hexane for a further 8 days and then had *M*, 264, m. p. 19·0° (47·6% of 10-bromo-acid).

Expt. J. Acetic acid. After 24 hours, the product appeared free from olefin but had *M*, 264 (calc., 265); the m. p. was 19·1° (47·8% of 10-bromo-acid). 0·2366 G. of 10-bromo-acid, mixed with 0·9981 g. of the product J, had m. p. 23·4°, whence 58·0% of 10-bromo-acid in the mixture and 48·1% in J.

Expt. K. Acetic acid. After 5 days the product had *M*, 264, m. p. 19·2° (48·0% of 10-bromo-acid). 0·3165 G. of 10-bromo-acid, mixed with 0·8417 g. of product K, had m. p. 24·9°, whence 62·0% of 10-bromo-acid in the mixture and 47·8% in K. The remainder of K was kept for a further 18 days with hydrogen bromide in acetic acid and then had *M*, 264, Br, 29·8 (calc., 30·2%) and m. p. 19·7° (49·0% of 10-bromo-acid).

Expt. L. Benzene. After 5 days the solution did not reduce permanganate and the product (yield 96%) had *M*, 265, Br, 30·0% and m. p. 20·05° (49·8% of 10-bromo-acid). Subjected to the action of hydrogen bromide in benzene solution for a further 5 days, this gave product L, which had *M*, 265, m. p. 20·05°. 0·6345 G. of product L, mixed with 0·2856 g. of 10-bromo-acid, had m. p. 26·0°, whence 65·1% of 10-bromo-acid in the mixture and 49·4% in L.

Expt. M. Benzene. After 5 days the product had m. p. 20·1° (50·0% of 10-bromo-acid). After 17 days, product M had *M*, 265, m. p. 20·05° (49·8% of 10-bromo-acid), Br, 30·2 (calc., 30·2%).

Expt. N. Hydrogen was passed for 30 minutes through a solution of diphenylamine (0·05 g.) and *iso*undecenoic acid (1·0 g., m. p. 18·7°) in pure benzene (20 c.c.) at 5°. Hydrogen bromide free from air was then passed for 1 hour (air being excluded) and the flask was sealed for 9 days. While the benzene was being evaporated in a vacuum diphenylamine hydrobromide crystallised and was removed. The product (1·3 g., m. p. 18·4°) was distilled and had m. p. 18·45° (46·5% of 10-bromo-acid). 0·6409 G. of product N, mixed with 0·3014 g. of 10-bromo-acid, had m. p. 25·5°, whence 63·7% of 10-bromoundecoic acid in the mixture and 46·7% in N.

Expt. O. A solution of perbenzoic acid (0·06 g.) and *iso*undecenoic acid (1·0 g., m. p. 18·7°) in pure benzene (20 c.c.) was kept for 40 minutes. It was then cooled to 5° while a slow stream of hydrogen bromide containing oxygen was passed for 1 hour. After 7 days the solvent was evaporated and the product (1·5 g.) was distilled, the first few drops (which contained benzoic acid) being rejected. The distillate, m. p. 17·6°, was redistilled and had m. p. 18·1°; again distilled, it had m. p. 18·2° (45·9% of 10-bromo-acid). 0·8257 G. of product O, mixed with 0·2767 g. of 10-bromo-acid, had m. p. 24·05°, whence 59·6% of 10-bromo-acid in the mixture and 46·1% in O.

TABLE I.

Expt.	Solvent.	Time, days.	Mol. wt. (calc., 265).	M. p.	10-Bromo-acid, mols. %.
A—H	Hexane / Benzene / Acetic acid	>9	264	19·9°	49·5
I	Hexane	2	262	18·3	46·2 (46·6) *
		10	264	19·0	47·6
J	Acetic acid	1	264	19·1	47·8
K	Acetic acid	5	264	19·2	48·0 (47·8)
		23	264	19·7	49·0
L	Benzene	5	265	20·05	49·8 (49·4)
		10	265	20·1	50·0
M	Benzene	5	—	20·1	50·0
		17	265	20·05	49·8
N	Benzene (+ H_2 + $NHPh_2$)	9	—	18·45	46·5 (46·7)
O	Benzene (+ O_2 + $Ph{\cdot}CO_3H$)	8	—	18·2	45·8 (46·1)

* Figures in parentheses are confirmations by addition of 10-bromo-acid.

Addition of Hydrogen Bromide to iso*Undecenoamide.*—Hydrogen bromide was passed through a solution of *iso*undecenoamide (3·0 g., m. p. 99·5°) in benzene (80 c.c.) at 25°, and the temperature gradually brought to 0°. After having stood 5 hours at 0°, the solution did not reduce permanganate; the solvent was removed at 35°. Conversion of the amido- into the carboxyl group was effected as follows: the viscous yellow residue was dissolved in a mixture of acetic acid (12 c.c.) and sulphuric acid (12 c.c. of 60%), and the solution cooled to 0°. While the solution was vigorously stirred, sodium nitrite (5 g. in 10 c.c. of water) was added during 1 hour. The mixture was then stirred for 1 hour at room temperature and finally for 10 minutes at 70°. After water had been added, the mixture was extracted three times with hexane; the bromo-acids were removed from the hexane solution by extraction with potassium hydroxide solution (5%) and liberated by addition of dilute sulphuric acid. The bromo-acids were again dissolved in hexane, the hexane evaporated, and the residue distilled.

Expt. X_1. The treatment with nitrous acid was less prolonged than described above and crystals of unchanged amide appeared in the distillate. These were removed by centrifuging and the clear oil, m. p. 17·4° (yield, 2·5 g.), was distilled. A few drops (b. p. < 150°/0·2 mm.) were rejected; the remainder (product X_1; yield, 2·2 g.) had *M*, 267·5, m. p. 18·0° (45·7% of 10-bromo-acid). 0·8995 G. of product X_1, mixed with 0·3441 g. of the 10-bromo-acid, had m. p. 24·5°, whence 61·0% of 10-bromo-acid in the mixture and 46·1% in product X_1.

Expt. X_2. The mixture of bromo-acids (2·6 g.) on distillation yielded 2·3 g. of light yellow oil, *M*, 266, m. p. 18·8° (47·1% of 10-bromo-acid). 0·9128 G. of product X_2, mixed with 0·3538 g. of 10-bromo-acid, had m. p. 24·9°, whence 62·0% of 10-bromo-acid in the mixture and 47·3% in X_2.

iso*Undecenol.*—A mixture of *iso*undecenoic acid (15 g., m. p. 18·7°), ethyl alcohol (100 c.c.), and hydrogen chloride (3 g.), heated under reflux during 12 hours, yielded 17 g. of ethyl *iso*undecenoate, b. p. 120°/0·2 mm. Reduction of the ester (15·3 g.) in dry alcohol (50 c.c.) with sodium (11 g.), followed by distillation in superheated steam, gave *iso*undecenol (9·6 g.; yield, 78%), b. p. 92°/0·1 mm. Chuit, Boelsing, Hausser, and Malet (*loc. cit.*, p. 1089) give b. p. 130°/13 mm. (Found: C, 77·6; H, 12·8. Calc.: C, 77·6; H, 12·9%).

Addition of Hydrogen Bromide.—Hexane was chosen as solvent because the mixture of bromo-undecanols separated within 5 hours and no conversion of $CH_2 \cdot OH$ into CH_2Br occurred. The speed of the reaction was surprising in view of the slow addition of hydrogen bromide to *iso*-undecenoic acid.

Hydrogen bromide was passed for 30 minutes into an ice-cold solution of *iso*undecenol (4·0 g.) in hexane (70 c.c.). When the mixture had stood for 3 hours at 0°, hydrogen bromide was passed for 10 minutes. After having stood for a total of 5 hours, the mixture had separated into two layers, both of which failed to reduce permanganate solution. The solvent was evaporated under reduced pressure, mainly at 0° and finally at 50°; yield, 5·9 g. A portion was distilled at 0·1 mm. for analysis (Found: Br, 31·9. Calc.: Br, 31·9%). Further preparations gave similar results.

Oxidation.—Nitric acid in any concentration was useless, and alkaline or neutral solutions of potassium permanganate caused loss of bromine. By the use of chromium trioxide in acetic acid in presence of potassium hydrogen sulphate (Willstätter, Mayer, and Hüni, *Annalen*, 1910, **378**, 104) yields of 50—70% were obtained, the loss being due mainly to esterification. Esterification also occurred during oxidation with sodium dichromate and 50% sulphuric acid.

Expt. Z_1. The mixture of bromoundecanols (5·2 g.) was suspended in sulphuric acid (100 c.c. of 50%) and stirred efficiently at 60°. Sodium dichromate (5 g., 1·2 mols.) in warm water (5 c.c.) was added gradually during ½ hour, and the mixture stirred ½ hour longer. The green liquid was extracted three times with hexane, the extract shaken with ice-cold potassium hydroxide solution (three times, each with 20 c.c. of 5% solution, which did not attack the bromine atoms), and the aqueous solution acidified. The bromo-acids, collected by complete extraction with hexane, were distilled (the first 3 drops being rejected), b. p. 149—156°/0·2 mm.; yield, 1·44 g., 26%. The m. p. (17·3°) indicated 44·3% of 10-bromoundecoic acid, but the product was not pure (Found: Br, 29·0; *M*, 266. Calc.: Br, 30·2%; *M*, 265).

Expt. Z_2. A solution of chromium trioxide (2·5 g., 1·2 mols.) in acetic acid (15 c.c.) and water (3 c.c.) was stirred at 50° along with finely powdered potassium bisulphate (3 g.). When the mixture of bromoundecanols (4·0 g., 1 mol.) in cold acetic acid (10 c.c.) was added in one portion, the temperature rose to 80°; it was then maintained at 90° for 10 minutes, dilute sulphuric acid (60 c.c. of 4%) added, and the mixture stirred for 5 minutes at 90°. The bromo-acids had b. p. 151—155°/0·2 mm. (yield, 2·3 g., 54%), *M*, 256·5, and m. p. 16·1°. The product was mixed with that from Z_3 (below).

Expt. Z_3. Another portion of the bromoundecanol mixture (5·0 g.), oxidised as in Z_2, gave 3·6 g. of distilled product, m. p. 15°; yield, 68% (the chromate liquor gave a slight reaction for bromide, indicating loss of bromine by hydrolysis). The distilled products Z_2 and Z_3 (5·5 g.) on fractional distillation gave 0·6 g., b. p. 120—151°/0·1 mm., and 4·6 g., b. p. 151—155°, *M*, 261, and m. p. 17·6°. On redistillation the second fraction gave 0·3 g., b. p. 151—152°, and 4 g., b. p. 152—155°, *M*, 261, Br, 29·1%, m. p. 17·6°: thus no separation from the impurity was effected. For a binary mixture of the bromo-acids, m. p. 17·6° corresponds to 45% of the 10-bromo-acid. 0·5161 G. of the mixture, added to 0·5275 g. of 10-bromo-acid, gave a new mixture, m. p. 28·5°, whence 45·2% of 10-bromo-acid in Z_2 + Z_3.

TABLE II.

Addition of Hydrogen Bromide to *iso*Undecenoamide in Benzene.

Product converted into 9- and 10-bromoundecoic acids.

Expt.	Yield, %.	*Mol. wt.* (calc., 265).	M. p.	*10-Bromo-acid,* mols. %.
X_1	73	267·5	18·0°	45·7 (46·1)
X_2	77	266	18·8	47·3

Addition of Hydrogen Bromide to *iso*Undecenol in Hexane.

Product converted into 9- and 10-bromoundecoic acids.

Expt.	Oxidising agent.	Yield, %.	Mol. wt.	M. p.	10-Bromo-acid, mols. %.
Z_1	$Na_2Cr_2O_7 + H_2SO_4$ *aq.*	26	267	17·3°	44·3
Z_2	CrO_3 + AcOH + $KHSO_4$	55 }	261	17·6	45·0 (45·2)
Z_3	,, ,,	68 }			

SUMMARY.

1. Addition of hydrogen bromide to *iso*undecenoic acid, $CH_3·CH{:}CH·[CH_2]_7·CO_2H$, yields 50% each of 9- and 10-bromoundecoic acids.

2. There is no "peroxide effect" * on the orientation, but the reaction appears to be fastest in benzene, a solvent which favours the "peroxide catalysed" reaction with *terminal* double bonds.

3. The solvent has no effect on the orientation of addition.

4. Conversion of the CO_2H group into $CO·NH_2$ or even into $CH_2·OH$ has no appreciable effect on the proportion of 9- and 10-bromo-compounds formed; the rate of addition, however, is much faster than to the acid.

5. A classification of reactivity in homologous series is given in which the reaction $CH_3·CH{:}CHR$ + HBr is classed as Type IV, the reactivity of the unsaturated carbon atoms being independent of the length of the alkyl chain.

6. 9-Ketoundecoic acid has been separated from the acids formed on hydration of undecynoic acid, and melts at 58—59°, not 43·5° (literature).

7. The binary system 9- and 10-bromoundecoic acids has been used for analysis of the addition products.

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* (*Note added, June 4th*, 1937). It has been shown by Harris and Smith (J., 1935, 1573) that with 10 : 11-undecenoic acid "molecular oxygen is essential to the 'peroxide' effect, and catalysts such as perbenzoic acid have a supplementary action." Urushibara and Takebayashi (*Bull. Chem. Soc. Japan*, 1937, **12**, 54) confirm this assertion by experiments with allyl bromide and state that dissolved oxygen is the active catalyst, but by quoting the sentence given above without the words "and catalysts such as perbenzoic acid have a supplementary action" they misinterpret the views of Harris and Smith. Oxygen *alone* will not in *all* circumstances bring about the so-called "peroxide" effect: pure undecenoic acid in hexane, for example, needs the *supplementary* action of such catalysts as water or epoxyundecoic acid. As it is agreed that molecular oxygen is the essential and the active catalyst, further confusion would be avoided by use of the term "oxygen" effect instead of "peroxide" effect.—J.C.S.

195. *The Benzylation of Aromatic Amines. Part V. The Reactions between* o-, m-, *and* p-*Cyanobenzyl Chlorides and Aniline, Ethylaniline, and Dimethylaniline.*

By D. H. PEACOCK and PO THA.

WITH aromatic amines *m*-nitrobenzyl chloride reacts faster than does the *p*-compound (Peacock, J., 1925, **127**, 2177; *J. Physical Chem.*, 1927, **31**, 535; Baker, J., 1933, 1128). With pyridine (Baker, J., 1936, 1448) and trimethylamine (Norrish and Smith, J., 1928, 129) the order is reversed. It seemed of interest to examine the rates of reaction of the cyanobenzyl chlorides with some aromatic amines, as the cyano-group, like the nitro-group, is a meta-directing substituent. Methyl alcohol was used as solvent.

TABLE I.

[Base] = 0·4*M*; [halide] = 0·1*M*.

Base.	Halide.	$k \times 10^3$ (35°).	$k \times 10^3$ (45°).
Aniline	Benzyl chloride	4·63	10·25
	o-Cyano- ,,	2·25	5·41
	m- ,, ,,	1·98	4·81
	p- ,, ,,	1·67	4·08
Ethyl-aniline	Benzyl chloride	5·76	12·90
	o-Cyano- ,,	2·03	4·56
	m- ,, ,,	2·13	4·77
	p- ,, ,,	1·82	4·12
Dimethyl-aniline	Benzyl chloride	3·50	7·92
	o-Cyano- ,,	0·63	1·47
	m- ,, ,,	0·88	1·90
	p- ,, ,,	0·75	1·73

TABLE II.

[Base] = 0·2*M*; [halide] = 0·05*M*.

Base.	Halide.	$k \times 10^3$ (30°).	$k \times 10^3$ (50°).
Aniline	Benzyl chloride	2·39	13·2
	o-Cyano- ,,	1·32	6·98
	m- ,, ,,	1·21	6·68
	p- ,, ,,	1·00	5·29
Ethyl-aniline	Benzyl chloride	3·40	17·7
	o-Cyano- ,,	1·13	5·71
	m- ,, ,,	1·25	6·65
	p- ,, ,,	0·98	5·11
Dimethyl-aniline	Benzyl chloride	2·25	11·2
	o-Cyano- ,,	0·32	1·69
	m- ,, ,,	0·49	2·69
	p- ,, ,,	0·36	2·02

With the three aromatic bases examined, *m*-cyanobenzyl chloride reacted faster than did the *p*-compound; the cyano-group thus resembles the nitro-group in this respect. The introduction of the cyano-group in any position lowers the rate of reaction. With the three bases examined, the factor governing the effect of the substituent seems to be its electron-attracting character; the greater this is, the slower is the rate of reaction.

The behaviour of *o*-cyanobenzyl chloride is interesting. Its rate of reaction is lower than that of benzyl chloride; with aniline, it is the fastest of the three cyano-compounds, with ethylaniline the second fastest, and with dimethylaniline the slowest. There is here the emergence of a steric effect not shown with aniline.

We thank the University of Rangoon for a grant.

UNIVERSITY COLLEGE, RANGOON. [*Received, April 19th, 1937.*]

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196. *The Liquid Acids of Sapucainha Oil.*

By HUMPHREY PAGET.

SAPUCAINHA oil is derived from the seeds of *Carpotroche brasiliensis*, Endl., and is used in Brazil for the treatment of leprosy. It resembles closely chaulmoogra and hydnocarpus oils, which are extensively used for the same purpose in other parts of the world, and it has been shown (da Silva, *Rev. Brasil. med. pharm.*, 1926, **2**, 627; Rothe and Surerus, *Rev. Soc. brasil. Chim.*, 1931, **2**, 358; Kariyone and Hasegawa, *J. Pharm. Soc. Japan*, 1934, **54**, 28) to yield the same characteristic acids, chaulmoogric and hydnocarpic, described by Power and his colleagues (J., 1904, **85**, 838; 1905, **87**, 884).

In addition to the crystalline components, the acids from these oils comprise a considerable liquid fraction, the composition of which has not been fully determined. Dean and Wrenshall (*J. Amer. Chem. Soc.*, 1920, **42**, 2626; *U.S. Pub. Health Bull.*, 1924, **141**, 15) obtained from the acids of chaulmoogra oil, by repeated distillation and by the solubility of the lead salts in ether, a liquid acid having an iodine absorption value 180·4, $[\alpha]_D$ + 53·1°,

M, 278·9. It gave no solid bromide, but yielded dihydrochaulmoogric acid on hydrogenation. They concluded that an acid, $C_{18}H_{30}O_2$, corresponding to chaulmoogric acid, but with a second ethylenic linkage, was present; from the manner in which it absorbed iodine they considered that the second ethylenic linkage was in the side chain. Hashimoto (*J. Amer. Chem. Soc.*, 1925, **47**, 2325) fractionated under 0·05 mm., in a specially designed apparatus, the final 10—15% of the ethyl esters of chaulmoogra oil which remained after removal of ethyl chaulmoograte and hydnocarpate, and which decomposed during distillation under 1—3 mm. He isolated taraktogenic acid, $C_{36}H_{60}O_6$, m. p. 113·5°, *iso*gadoleic acid, $C_{20}H_{38}O_2$, m. p. 65·6—66°, a lactone-like substance, $C_{18}H_{32}O_2$, m. p. — 11·6°, and other less definite products, which included a considerable amount of tarry matter.

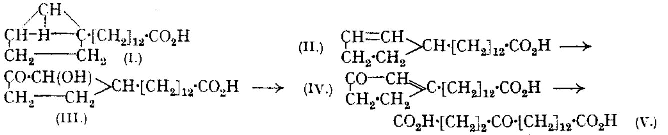
The present work deals with the liquid acids from sapucainha oil, but the conclusions apply equally to the corresponding fraction of acids from hydnocarpus oil. In order to minimise decomposition and polymerisation of these rather unstable acids, separation by distillation was avoided as far as possible, and recourse had to crystallisation and to the separation of the copper salts by means of their different solubilities in acetone and in ether. In this way the residual acids from the mother-liquors after crystallisation of the total acids were separated into three principal fractions :

1. Crystalline acids derived from acetone-insoluble, ether-soluble copper salts. These consisted of chaulmoogric, hydnocarpic and palmitic acids.

2. Liquid acids, soluble in light petroleum, derived from acetone-soluble copper salts, and containing chaulmoogric, hydnocarpic, palmitic, *ketochaulmoogric*, *ketohydnocarpic*, oleic and *dehydrochaulmoogric* acids.

3. Tarry acids, insoluble in light petroleum, derived from the copper salts insoluble in acetone and in ether, and from which a small quantity of ketochaulmoogric and ketohydnocarpic acids was isolated.

The liquid acids deposited on standing a small crystalline crust, from which, by fractional distillation of the methyl esters, palmitic acid and a mixture of two optically inactive keto-acids were obtained. The keto-acids were separated with difficulty into ketochaulmoogric acid (IV), $C_{18}H_{30}O_3$, m. p. 116°, and a small amount of an acid, $C_{16}H_{26}O_3$, m. p. 108°, apparently the lower homologue, ketohydnocarpic acid. The first of these gave on catalytic hydrogenation (1·7 mols. of hydrogen) a mixture of dihydrochaulmoogric acid and a *dihydroketo-acid*, and on oxidation γ-keto-n-pentadecanedicarboxylic acid (V) in large yield.



In the course of unpublished work carried out in these laboratories in 1916 on the acids of chaulmoogra oil, Clewer isolated an optically inactive acid, m. p. 114—115°, for which he suggested the formula $C_{18}H_{30}O_3$. His acid was not available for comparison, but from the details of its isolation it is likely that it was identical with ketochaulmoogric acid. Barrowcliff and Power (J., 1907, **91**, 557) found γ-keto-n-pentadecanedicarboxylic acid among the products of oxidation of chaulmoogric acid and were thus led to formulate chaulmoogric acid as in a state of equilibrium between two tautomeric forms (I). Perkins (*J. Amer. Chem. Soc.*, 1926, **48**, 1714), while agreeing with Shriner and Adams (*ibid.*, 1925, **47**, 2727) that formula (II) is sufficient to explain Barrowcliff and Power's results, could yet find no intermediate products to account for the production of γ-keto-n-pentadecanedicarboxylic acid. Its ready formation from ketochaulmoogric acid (IV), and the fact that the latter has also been prepared by the autoxidation of chaulmoogric acid or its ethyl ester, suggest the above course of oxidation, the keto-acid being a dehydration product of the ketol (III), which, though it has not been isolated, may be supposed to be formed during autoxidation (cf. King, J., 1936, 1788).

The remainder of the liquid acids, about 16% of the total acids, contained a more highly unsaturated constituent than chaulmoogric acid, and this has been identified as dehydrochaulmoogric acid (VI).

$$\text{(VI.)}\quad \left.\begin{array}{l}CH{=}CH\\ CH_2{\cdot}CH_2\end{array}\right\rangle CH{\cdot}[CH_2]_6{\cdot}CH{:}CH{\cdot}[CH_2]_4{\cdot}CO_2H \longrightarrow$$

$$\text{(VII.)}\quad \left.\begin{array}{l}CH(OH){\cdot}CH(OH)\\ CH_2\text{———}CH_2\end{array}\right\rangle CH{\cdot}[CH_2]_6{\cdot}[CH(OH)]_2{\cdot}[CH_2]_4{\cdot}CO_2H \longrightarrow$$

$$\text{(VIII.)}\quad CO_2H{\cdot}[CH_2]_2{\cdot}CH(CO_2H){\cdot}[CH_2]_6{\cdot}CO_2H + CO_2H{\cdot}[CH_2]_4{\cdot}CO_2H \quad \text{(IX.)}$$

Dehydrochaulmoogric acid yielded no crystalline derivative by which it could be isolated, and since further purification involved distillation at a somewhat high temperature and with decomposition, it was not attempted. On the basis of the iodine absorption value and on the assumption that oleic and chaulmoogric are the only other acids present, it constituted about 60% of this fraction of acids. The liquid acids were readily hydrogenated, yielding dihydrochaulmoogric and stearic acids. The products of oxidation by permanganate included (i) dihydroxystearic acid, which with the formation of stearic acid by hydrogenation proved the presence of oleic acid, and (ii) a lævorotatory, water-soluble acid, which for the reasons given below is regarded as *tetrahydroxydihydrochaulmoogric acid* (VII). This acid can exist in a number of stereoisomeric forms and the fact that difficulty was experienced in raising the melting point by crystallisation, and that fractions melting as widely apart as 60° and 113° gave comparable analytical figures and the same products on oxidation, suggests the presence of more than one form. It was rapidly oxidised by cold Beckmann's chromic acid mixture to give adipic acid (IX) and a tribasic acid, $C_{12}H_{20}O_6$, which could not be obtained crystalline but yielded a *trianilide*. The tribasic acid must be n-*nonane*-$\alpha\alpha'\gamma$-*tricarboxylic acid* (VIII), since on oxidation succinic acid and a mixture of adipic and suberic acids were obtained.

In addition to the tribasic acid (VIII) a keto-acid was isolated from the oxidation products of tetrahydroxydihydrochaulmoogric acid, as its *semicarbazone*, $C_{13}H_{23}O_5N_3$. Insufficient was obtained to determine its constitution, but by analogy with δ-keto-*n*-hexadecanedicarboxylic acid, obtained by Shriner and Adams (*loc. cit.*) from *iso*chaulmoogric acid, it is possible that this acid is δ-keto-*n*-decane-αω-dicarboxylic acid, $CO_2H{\cdot}[CH_2]_3{\cdot}CO{\cdot}[CH_2]_6{\cdot}CO_2H$, indicating the presence of a dehydro*iso*chaulmoogric acid in the liquid acid fraction.

The acid fraction (3) from the copper salt insoluble in acetone and in ether resembled the non-crystalline products obtained by autoxidation of sapucainha oil, its acids or their esters. Like other unsaturated long-chain fatty acids, after long exposure to light and air in thin layers they exhibit a rise in acid and saponification values and of specific gravity, and a considerable lowering of iodine absorption value and specific rotation. From the clinical point of view this product is of importance, since it causes great irritation on injection (Paget, Trevan, and Attwood, *Internat. J. Leprosy*, 1934, **2**, 149), and hydnocarpus preparations, intended for clinical use, should be prepared and stored under conditions which will reduce the risk of autoxidation, with the formation of this substance, to a minimum.

The amounts of these constituents in the sample of oil examined were approximately (i) chaulmoogric, hydnocarpic and palmitic acids 65—70%, (ii) oleic acid 4%, (iii) dehydrochaulmoogric acid 9%, (iv) ketochaulmoogric and ketohydnocarpic acids 4%, and (v) tarry acids 9%.

EXPERIMENTAL.

Isolation of Acids of Sapucainha Oil.—The seeds of *Carpotroche brasiliensis* resembled those of *Hydnocarpus wightiana* but were smaller, 100 seeds weighing on an average 34 g. They were crushed and extracted completely with carbon tetrachloride. The extract was evaporated, and the residue freed from traces of solvent by steam and dried at 100° in a vacuum. The yield of oil was 41·2% of the whole seed, and it closely resembled hydnocarpus oil.

Oil.	Acid value.	Sapon. value.	Iodine value.	$[\alpha]_D$.	$d_{25^\circ}^{25^\circ}$.
Sapucainha	21·7	199·7	101·3	+54·0°	0·9563
Hydnocarpus	6·0	196·0	95·0	+55·4	0·9656

The oil was hydrolysed by boiling for 30 minutes with a small excess of *N*-alcoholic potash; most of the alcohol was then distilled off, and the residue diluted with water and acidified. The fatty acids were washed with water, dried at 100°, and dissolved in 10 volumes of 80% alcohol. After standing overnight at 10°, a crop of crystalline acids separated (*A*; 56·5%). It has been repeatedly shown that the mixture of crystalline acids isolated from chaulmoogra and hydnocarpus oils consists essentially of chaulmoogric and hydnocarpic acids and small amounts of palmitic acid have also been obtained (Power and Gornall, J., 1904, **85**, 838). The crystalline acids of sapucainha oil have the character of such a mixture, m. p. 44—46°, $[\alpha]_D$ + 57·2°, and by fractional crystallisation from alcohol of strength gradually increasing from 80 to 95%, and finally from light petroleum, these three components were separated, chaulmoogric acid, m. p. 69°, $[\alpha]_D^{20°}$ + 62·05° (*c* = 1·04; chloroform); hydnocarpic acid, m. p. 56°, $[\alpha]_D^{20°}$ + 67·7° (*c* = 0·76; chloroform); palmitic acid, m. p. 62°.

Evaporation of the mother-liquors from the crystalline acids left a soft, light brown solid (43·5%; acid value, 195; iodine value, 129; $[\alpha]_D$ + 52°). This was dissolved in alcohol and neutralised by alcoholic potassium hydroxide, and the solution evaporated to dryness at low pressure. The dried potassium salts were extracted with acetone, which removed a small amount of unsaponified oil and a neutral substance crystallising from *iso*propyl ether in leaflets, m. p. 132°; it gave the colour reactions of the phytosterol isolated by Power and Gornall (*loc. cit.*) from chaulmoogra oil, and a mixture with this substance showed no depression of melting point. From the potassium salts, dissolved in water, the copper salts were precipitated by a solution of copper acetate as a plastic mass, which was washed with water, air-dried, and ground with successive quantities of cold acetone until the solvent remained colourless. On evaporation of the acetone, about 75% of the copper salt remained as a sticky, dark green mass (acetone-soluble copper salt). The acetone-insoluble fraction was refluxed with ether, which removed a small amount (ether-soluble copper salt) as a dark green powder on evaporation of the solvent. Finally a lighter coloured solid salt remained, insoluble both in acetone and in ether (insoluble copper salt). Each of these three fractions was decomposed by shaking with a small excess of 10% hydrochloric acid and an equal volume of ether until dissolved, and the acid recovered. The ether-soluble copper salt yielded a mixture of crystalline acids closely resembling (*A*), with which it was mixed, and it need not be further considered.

Acids from the Acetone-soluble Copper Salt.—The acid from the acetone-soluble copper salt was a light brown, rather viscous oil. It was poured into 15 volumes of light petroleum and shaken with charcoal, which eliminated a small amount of tar; after standing for some days at about 4°, the solution was decanted and evaporated, yielding a liquid, golden-yellow acid fraction, which slowly deposited crystalline matter (*B*). When the deposition ceased, the clear liquid acids were decanted and converted into methyl esters, and the latter distilled in a current of carbon dioxide until the b. p. rose to 200°/4 mm.; distillation was then stopped. The distilled fractions (30%; saponification value, 195 to 200; $[\alpha]_D$ + 40° to + 50°) on hydrolysis yielded solid acids, which, after removal of a crop of nearly pure hydnocarpic acid by crystallisation from alcohol, were mixed with (*B*). The undistilled fraction of methyl esters, after hydrolysis and removal of a little crystalline acid, which proved to be mainly chaulmoogric acid, yielded the liquid acid fraction, as a mobile yellow oil, which solidified to some extent below 5° (*C*; 16% of total sapucainha acids; acid value, 198; iodine absorption value, 138; $[\alpha]_D$ + 45°).

Acid fraction (B). The crystalline matter (*B*) was converted into the methyl ester and distilled in three fractions: (1) b. p. 145—160°/0·5 mm. (30%); (2) b. p. 160—185°/0·5 mm. (34%); (3) b. p. 185—210°/0·5 mm. (12%), leaving a tar which decomposed on further heating. Fraction (1) solidified and after crystallisation from methyl alcohol was identified by its m. p. (29°) and that of its acid (62°) as methyl palmitate. Fraction (2) was a mixture. The third fraction also crystallised, m. p. about 42°, and yielded on hydrolysis an optically inactive acid, sparingly soluble in ether, m. p. 98—104°. After repeated crystallisation from alcohol, ethyl acetate and finally from acetic acid, it was obtained in slightly yellow, crystalline granules, m. p. 116° (Found: C, 73·5; H, 10·2. $C_{18}H_{30}O_3$ requires C, 73·5; H, 10·2%). It yielded a *semicarbazone*, which crystallised well from alcohol, m. p. 157° (decomp.) (Found: C, 65·3; H, 9·45; N, 11·85. $C_{19}H_{33}O_3N_3$ requires C, 64·95; H, 9·4; N, 11·95%), and on acid hydrolysis gave the original keto-acid, which is shown below to be ***ketochaulmoogric acid***.

From the mother-liquors from which this acid was obtained a small amount of another acid separated, m. p. 108°, which appeared to be the lower homologue, ***ketohydnocarpic acid*** (Found: C, 72·3; H, 9·1. $C_{16}H_{26}O_3$ requires C, 72·2; H, 9·8%), but insufficient was obtained from this source in a pure condition to characterise it beyond the preparation of its ***semicarbazone***, m. p. 156° (decomp.) (Found: C, 63·45; H, 8·9; N, 12·5. $C_{17}H_{29}O_3N_3$ requires C, 63·2; H, 9·0; N, 13·0%).

Ketochaulmoogric acid **(IV).** When shaken vigorously in alcoholic solution with Adams's platinum oxide catalyst in hydrogen, the keto-acid absorbed rather less than the equivalent of two molecules (Found, 1 g. = 130·7 c.c. Calc. for $2H_2$, 152·4 c.c.). The m. p. of the product was indefinite, 74—82°, and by treatment with semicarbazide and refluxing the product with ether it was separated into an insoluble *semicarbazone* (60%), m. p. 164° (from acetic acid) (Found : C, 64·85; H, 10·0; N, 11·7. $C_{19}H_{35}O_3N_3$ requires C, 64·6; H, 9·9; N, 11·9%), and an ether-soluble non-ketonic acid (40%), m. p. and mixed m. p. with dihydrochaulmoogric acid, 72° (Found : C, 76·0; H, 12·0. Calc. : C, 76·6; H, 12·1%). The keto-acid (0·7 g.) in 1% potassium hydroxide solution (20 c.c.) was oxidised at 20° by 1% aqueous potassium permanganate (120 c.c.), and the filtered solution made acid and extracted with ether. It yielded an acid, m. p. and mixed m.p. with γ-keto-*n*-pentadecanedicarboxylic acid 127° (Found: C, 65·1; H, 9·5. Calc.: C, 65·0; H, 9·55%). This identification was confirmed by preparation of the oxime, m. p. 87°.

The liquid acids (C). *Hydrogenation.* On hydrogenation in alcoholic solution in presence of palladium on barium sulphate, the liquid acids absorbed rapidly 40% of the amount of hydrogen required by the iodine value (Found : 48 c.c. per g.; required by iodine value 138, 122 c.c. per g.), yielding (*a*) a crystalline acid, m. p. and mixed m. p. with dihydrochaulmoogric acid 72°, and (*b*) a non-crystalline residue, iodine value 86, $[\alpha]_D$ — 0·6°. The latter rapidly absorbed more hydrogen in presence of Adams's platinum oxide catalyst (Found : 83 c.c. per g.; required by iodine value 86, 76 c.c. per g.), yielding a solid, optically inactive product, which crystallised well from light petroleum in leaflets. Prolonged fractional crystallisation resulted in the isolation of nearly 50% as dihydrochaulmoogric acid, the remaining crops melting between 48° and 65° and being of almost the same empirical composition (Found : C, 76·1; H, 12·3; *M*, by titration, 296·3. Calc. : C, 76·6; H, 12·1%; *M*, 282). They showed no depression of m. p. with a mixture of dihydrochaulmoogric acid (70%) and stearic acid (30%), which melted at 63—64°. No further separation could be effected by distillation of the methyl esters, by lead salt precipitation, or by crystallisation of the *p*-bromoanilides, which melted at 93° to 96° after several crystallisations from light petroleum (Found : C, 66·0; H, 8·85; N, 3·5; Br, 18·4. Calc. for $C_{24}H_{38}ONBr$: C, 66·0; H, 8·7; N, 3·2; Br, 18·35%). The p-*bromoanilide* of dihydrochaulmoogric acid melts at 102° and that of stearic acid at 113°; a mixture in the proportion 70 : 30 melts at about 95—100°.

Oxidation. The liquid acids (50 g.) in 10% potassium hydroxide solution (300 c.c.) and 1 l. of water were oxidised by 4% aqueous potassium permanganate (1 l.), added slowly and with vigorous stirring, about 1 kg. of ice being added during the operation. Sulphur dioxide was passed into the product to decompose the manganese dioxide, and the solution made acid to Congo-red paper and kept. The aqueous layer was separated from water-insoluble acids, which were boiled with 1500 c.c. of water and separated. The water-insoluble acids were dissolved in ether, dried, and diluted with the same solvent; a flocculent precipitate then separated. After crystallisation from ethyl acetate, it had m. p. and mixed m. p. with dihydroxystearic acid, 131° (Found: C, 68·1; H, 11·2. Calc.: C, 68·4; H, 11·4%). The remaining water-insoluble, syrupy product (acid value, 175; iodine absorption value 50, $[\alpha]_D$ + 5°) was not further examined.

The combined aqueous solutions were concentrated till opalescent, and on cooling they deposited a flocculent solid; this was filtered off, and the process repeated, until about 100 c.c. remained, which were extracted with ether. The acid so obtained was sparingly soluble in ether, chloroform or benzene, moderately in water or ethyl acetate and readily in alcohol; by repeated crystallisation from ethyl acetate and finally from water, an *acid* was obtained, m. p. 111—113°, $[\alpha]_D^{18°}$ — 17·9° (c = 1·7; absolute alcohol) (Found: C, 62·55; H, 10·1; *M*, by titration, 349·7. $C_{18}H_{34}O_6$ requires C, 62·4; H, 9·8%; *M*, 346). The *methyl* ester, prepared by means of diazomethane, was rather sparingly soluble in ether, but crystallised well from benzene, m. p. 88° (Found : C, 63·2; H, 10·45; OMe, 8·4. $C_{19}H_{36}O_6$ requires C, 63·3; H, 10·0; OMe, 8·6%). On heating a few degrees above the m. p. for some hours, the acid lost 4·8% (H_2O requires 5·2%), forming a glassy lactone, from which the acid was regenerated by long boiling with potassium hydroxide in alcohol. The acid did not react with semicarbazide; attempts to obtain a crystalline benzoate or nitrobenzoate were unsuccessful, the greater part of the acid being recovered apparently as the lactone. The methoxyacetyl derivative of the methyl ester was prepared by heating the ester (1 g.) in dry pyridine (5 c.c.) with methoxyacetic anhydride (5 g.) to boiling for 1 minute : after standing for 2 hours, the product was dissolved in ether and washed several times with 1% sulphuric acid and with 2% sodium carbonate solution. The product, which was a hygroscopic syrup, was dried to constant weight in a vacuum desiccator [Found : C, 57·8; H, 8·1; OMe, 23·1; *M* (by hydrolysis), 657. $C_{19}H_{32}O_6(C_3H_5O_2)_4$ requires C, 57·4; H, 8·0; OMe, 23·9%; *M*, 648]. This is therefore the *tetramethoxyacetyl* derivative of methyl tetra-

hydroxydihydrochaulmoograte. The *phenylurethane* of the acid, prepared by refluxing with the theoretical amount of phenyl *iso*cyanate in dry benzene solution for 6 hours, crystallised from dilute alcohol, m. p. 145° [Found : C, 67·5; H, 6·6; N, 7·15. $C_{18}H_{30}O_6(C_7H_6ON)_4$ requires C, 67·15; H, 6·6; N, 6·8%].

Oxidation of Tetrahydroxydihydrochaulmoogric Acid (VII).—The acid (2 g.) was heated gently with Beckmann's chromic acid mixture (80 c.c.) for 15 minutes, cooled, and extracted thoroughly with ether. The product was allowed to crystallise from about 3 c.c. of ether, yielding an acid, m. p. 151°, identified as adipic acid (Found : C, 49·75; H, 7·0. Calc. : C, 49·3; H, 6·85%). It was further identified by the dianilide, m. p. 238°, and the bromophenacyl ester, m. p. 154°. The yield of adipic acid isolated was about 35% (calc., 42·2%).

The rest of the oxidation product did not solidify. With an alcoholic solution of semicarbazide, it yielded a very small amount of a *semicarbazone*, m. p. 187° (Found : C, 51·1; H, 7·6; N, 13·9. $C_{13}H_{23}O_5N_3$ requires C, 51·8; H, 7·65; N, 13·95%). The non-ketonic acid was recovered, esterified by diazomethane, and distilled to remove traces of methyl adipate; a fraction was obtained, b. p. 200—217°/15 mm., which did not crystallise [Found : C, 59·85; H, 8·75; OMe, 29·5. $C_9H_{17}(CO_2Me)_3$ requires C, 59·6; H, 8·6; OMe, 30·8%]. The *trianilide* was prepared from the methyl ester by Hardy's method (J., 1936, 398), m. p. 189° (from absolute alcohol) (Found : C, 73·95; H, 7·35; N, 8·85. $C_{30}H_{35}O_3N_3$ requires C, 74·2; H, 7·2; N, 8·65%).

Oxidation of the Tribasic Acid, $C_{12}H_{20}O_6$ (VIII).—The tribasic acid (3 g.) was refluxed for 24 hours with successive amounts of Beckmann's chromic acid mixture (30 c.c.), and the combined liquors extracted thoroughly with ether. A mixture of crystalline acids was obtained in addition to unchanged tribasic acid, and on boiling with chloroform a part was sparingly soluble, m. p. and mixed m. p. with succinic acid 181°; its *p*-bromophenacyl ester melted at 210°; and it gave a sparingly soluble, crystalline barium salt (Found : Ba, 54·75. Calc. for $C_4H_4O_4Ba$: Ba, 54·2%). From the fraction of acids soluble in chloroform was separated, by repeated crystallisation from ethyl acetate, a small amount which, though melting sharply at 122—123°, was apparently a mixture (Found : C, 53·4; H, 7·65; *M*, by titration, 168). A mixture of suberic acid (70%) and adipic acid (30%), fused together and finely powdered, melted at 121—123° (Calc. : C, 53·35; H, 7·65%; *M*, 165·6); admixture with the acid from the oxidation caused no change of m. p.

The Acids from the "Insoluble Copper Salt."—The product from the decomposition of the insoluble copper salt by dilute hydrochloric acid was dark and viscous and represented about 9% of the total acids. It gave a barium salt insoluble in water and had acid value 151, saponification value 226, iodine absorption value 69, $[\alpha]_D$ about + 10°. Neither the acids nor their ethyl esters could be distilled without considerable decomposition; a part of the ethyl esters was soluble in light petroleum but gave no appearance of satisfactory separation. When the acid was boiled with light petroleum, and the solvent decanted hot and kept, a small amount of a mixture of ketochaulmoogric and ketohydnocarpic acids separated, but no other crystalline product was obtained.

Autoxidation of Sapucainha Oil and of Ethyl Chaulmoograte.—Sapucainha oil was exposed in thin layers in glass dishes to sunlight and air for several months. The oil, which was at first limpid, gradually set to a tough and sparingly soluble skin, without darkening in colour. On saponification it at once became very dark, yielding a tarry acid product.

Ethyl chaulmoograte, prepared from pure chaulmoogric acid and distilled in carbon dioxide at 191—193°/0·5 mm., melted at 8°, saponification value, 184·5; iodine absorption value, 82·3; $[\alpha]_D^{20^\circ}$ + 56·3° (c = 1·03; chloroform); $d_{15^\circ}^{15^\circ}$ 0·9080. This was freely exposed in the same way throughout the summer months; it then showed an increase in weight of 8·5% (calc. for O_2, 10·4%), and was considerably altered in character [acid value, 27·7; saponification value, 211·6; iodine absorption value, 31·8; $[\alpha]_D^{20^\circ}$ + 3·3° (c = 1·17; chloroform); $d_{15^\circ}^{15^\circ}$ 1·002]. The product was hydrolysed by dissolving it in alcohol, and, in an atmosphere of nitrogen, adding the calculated amount of alcoholic potassium hydroxide solution. The solution darkened at once; it was concentrated and acidified, and the syrupy acid product dried and extracted repeatedly with hot light petroleum. The petroleum extract deposited crystals, separating from alcohol in a granular form, m. p. and mixed m. p. with ketochaulmoogric acid from the liquid acid fraction of sapucainha oil, 116°.

The author is indebted to Dr. T. A. Henry for valued criticism and advice, and to Messrs. A. Bennett and H. C. Clarke for micro-analyses.

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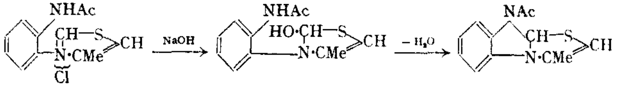
197. *Substituted Phenyl- and Benzyl-thiazolium Salts.*

By Karimullah.

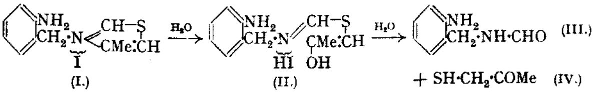
In the course of experiments on the synthesis of aneurin, attempts were made to prepare a substance having a constitution like that originally proposed for this vitamin by Williams (*J. Amer. Chem. Soc.*, 1935, **57**, 229), but having a phenyl instead of a pyrimidine nucleus. Such an analogue would be *N*-*o*-aminophenylthiazolium chloride, for which monothioformyl-*o*-phenylenediamine could serve as a point of departure. The latter substance could, however, not be prepared because the thioformylation of *o*-phenylenediamine leads to benzimidazole (Todd, Bergel, Karimullah, and Keller, this vol., p. 361). Therefore monoacetyl-*o*-phenylenediamine was thioformylated and then condensed with chloroacetone, to form a thiazolium chloride. Attempts to deacetylate the product with sodium hydroxide and subsequent treatment in ether with hydrogen chloride gave a crystalline salt of a tertiary base isomeric with the original substance. The new salt may be a dihydrothiazole hydrochloride and it might be formed according to the following scheme :



On oxidation with potassium ferricyanide in alkaline solution, no fluorescence was observed.

After the present formula for aneurin had been put forward and confirmed by synthesis (Williams and Cline, *J. Amer. Chem. Soc.*, 1936, **58**, 1504 ; Todd and Bergel, this vol., p. 364) similar experiments were made with a view to obtaining *N*-*o*-aminobenzylthiazolium chloride. *o*-Aminobenzylamine on thioformylation yields dihydroquinazoline in quantitative yield (Todd, Bergel, Karimullah, and Keller, *loc. cit.*). The hydrochloride of *o*-aminobenzyl chloride, on treatment with 4-methylthiazole, merely yielded the highly polymerised product $\left(C_6H_4{<}{NH \atop CH_2}\right)_n$ recorded by Gabriel and Posner (*Ber.*, 1894, **27**, 3514). Hence reduction of N-*o*-*nitrobenzyl-4-methylthiazolium chloride* was resorted to, hydriodic acid and red phosphorus being found to be the most suitable agent. The *iodide* formed, being rather unstable, was converted into the corresponding *chloride.* On alkaline oxidation with potassium ferricyanide, this compound gave a blue fluorescence in ultraviolet light, but a crystalline substance like thiochrome could not be separated.

Alkaline oxidation of this iodide with potassium ferricyanide invariably gave iodoform, and when the same operation was repeated with other *N*-phenyl- or -benzyl-thiazolium iodides, a very strong smell of *iso*nitrile was detected. This could be explained as follows :



(I.) (II.) (III.) (IV.)

(III) closes to form a dihydroquinazoline, which would be dehydrogenated to quinazoline, and (IV) gives iodoform with iodine set free from sodium iodide by potassium ferricyanide during the reaction. In the case of other *N*-phenylthiazolium iodides having no *o*-amino-group, the formyl group is further hydrolysed, giving a primary amine, which reacts with iodoform in an alkaline medium to form the *iso*nitrile.

Thiochrome could not be obtained quantitatively by oxidation of aneurin (compare Barger, Bergel, and Todd, *Ber.*, 1935, **68**, 2257), the yield being at the most 70%. It is suggested that a side reaction as stated above might lead to destruction of a good deal of aneurin.

Attempts to prepare a phenyl analogue of thiochrome by condensing *o*-chlorobenzyl chloride with 2-amino-4-methylthiazole according to Todd, Bergel, Fraenkel-Conrat, and Jacob (J., 1936, 1601) were without success. Presumably the chloromethyl group

reacts preferentially with the amino-group of the thiazole; moreover the chlorine in a benzene ring would be less reactive than when attached to the 6-position of a pyrimidine ring.

EXPERIMENTAL.

N-o-*Acetamidophenyl-4-methylthiazolium Chloride.*—Monoacetyl-*o*-phenylenediamine was prepared according to Leuchs (*Ber.*, 1907, **40**, 1084), but the tin was removed by hydrogen sulphide. Yield, 58%.

Thioformylmonoacetyl-*o*-phenylenediamine (5 g.) was dissolved in acetone (300 c.c.) by heating and, after cooling, chloroacetone (5 c.c.) was added. The mixture was kept overnight at room temperature and subsequently refluxed for 2 hours, and the acetone evaporated. The residue, after digestion with ether to remove unchanged material, crystallised from methanol-acetone (charcoal) in colourless plates, m. p. 222°. Yield, about 85% (Found: C, 53·8; H, 4·9; S, 11·5. $C_{12}H_{13}ON_2ClS$ requires C, 53·6; H, 4·8; S, 11·9%).

In all these condensations acetone proved to be a useful solvent. In alcoholic solution the thioformyl group was often hydrolysed and 2-methylbenzimidazole was obtained instead of a thiazolium salt. The *hydrochloride* of the tertiary base got by treatment with dilute sodium hydroxide solution had m. p. 188° (Found: C, 54·1; H, 4·9; S, 11·4; Cl, 13·4. $C_{12}H_{12}ON_2S$,HCl requires C, 53·6; H, 4·8; S, 11·9; Cl, 13·2%).

N-*o*-Tolyl-4-methylthiazolium chloride, prepared as above from thioformo-*o*-toluidide (1 g.) and chloroacetone (1·2 g.) in acetone (30 c.c.), was converted by potassium iodide into the *iodide*, m. p. 230° (decomp.) after crystallisation from alcohol–ether. Yield, 90% (Found: C, 42·1; H, 4·1; S, 9·6. $C_{11}H_{12}NIS$ requires C, 41·7; H, 3·8; S, 10·0%).

N-*Benzyl-4-methylthiazolium Chloride.*—Thioformylbenzylamine, condensed with chloroacetone in equivalent amount in the usual manner, gave a *chloride* which showed no depression in m. p. when mixed with that obtained from benzyl chloride and 4-methylthiazole; m. p. 188° (Found: N, 6·1. $C_{11}H_{12}NClS$ requires N, 6·2%).

Similarly, *N-o-nitrobenzyl-4-methylthiazolium chloride* obtained from thioformyl-*o*-nitrobenzylamine and chloroacetone was identical with that from *o*-nitrobenzyl chloride and 4-methylthiazole; m. p. 200° (Found: N, 10·0. $C_{11}H_{11}O_2N_2ClS$ requires N, 10·3%).

N-o-*Chlorobenzyl-4-methylthiazolium Chloride.*—*o*-Chlorobenzyl chloride (3·5 g.) was heated with 4-methylthiazole (2·5 g.) on a water-bath for 2 hours. The crystalline mass was washed with ether and recrystallised from alcohol–ether; m. p. 190° (decomp.). Yield, 4 g. (Found: C, 50·3; H, 4·5; Cl, 26·8. $C_{11}H_{11}NCl_2S$ requires C, 50·7; H, 4·2; Cl, 27·3%).

2-o-*Chlorobenzylamino-4-methylthiazole hydrochloride*, prepared from *o*-chlorobenzyl chloride and 2-amino-4-methylthiazole as above, crystallised from ethyl alcohol–ether in colourless needles, m. p. 260° (decomp.) (Found: C, 48·4; H, 4·5; Cl, 25·5. $C_{11}H_{11}N_2ClS$,HCl requires C, 48·0; H, 4·4; Cl, 25·8%). The free base melted at 100°. The hydrochloride and the free base showed bluish-violet fluorescence in ultra-violet light.

2-o-*Chlorobenzylaminothiazole hydrochloride*, prepared from *o*-chlorobenzyl chloride and 2-aminothiazole, had m. p. 245° (Found: C, 46·3; H, 3·9. $C_{10}H_9N_2ClS$,HCl requires C, 46·0; H, 3·8%). The free base had m. p. 58°.

N-o-*Aminobenzyl-4-methylthiazolium Chloride Hydrochloride.*—Hydriodic acid (*d* 1·7; 8 c.c.) and red phosphorus (0·5 g.) were heated nearly to boiling. After removal of the flame *N*-*o*-nitrobenzyl-4-methylthiazolium chloride (1·5 g.) was added in portions. On each addition a slight reaction ensued. The whole was boiled for ½ hour. After cooling, the crystalline mass was collected on fritted glass filter and recrystallised from water containing a little hydriodic acid; m. p. 237° (decomp.). The crystals assumed a brownish-yellow colour on exposure to light. The *salt* was readily hydrolysed and each successive recrystallisation lowered the m. p. and the iodine content (Found: I, 54·6. $C_{11}H_{14}N_2I_2S$ requires I, 55·2%).

The *chloride* was found to be more stable and was prepared by shaking the iodide with freshly precipitated silver chloride in methanol for 4 hours. The filtrate was treated with excess of dry ether; the chloride crystalled in colourless needles, m. p. 213° (decomp.) (Found: N, 9·9; Cl, 25·7. $C_{11}H_{14}N_2Cl_2S$ requires N, 10·1; Cl, 25·7%).

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198. "*Green*" *Ethyl Tartrate.*

By T. S. Patterson and Alexander H. Lamberton.

It was suggested by Patterson (J., 1922, **121**, 1042) that the slight yellow colour sometimes acquired by ethyl tartrate when hot, and lost after a few hours (Lowry and Cutter, *ibid.*, p. 537), might be due to an oxidation product, since it could easily be produced in colourless ethyl tartrate by passage of air through the hot ester. We have investigated this matter further.

Various experiments were made to concentrate this oxidation product as far as possible. About 250 g. of ethyl tartrate were heated to 200° in a Claisen flask, the side neck of which was lengthened, and contained a rod and disc fractionating column. Air was sucked through the hot ester for some 5 minutes at ordinary pressure. Then, at reduced pressure, a small first fraction, which was highly coloured (brownish-yellow), was carefully distilled off. The whole process was repeated some 20 times, until about 150 g. of distillate had been collected. This had $\alpha_{5461}^{22^\circ}$ (100 mm.) + 10°. On redistillation, a colourless, inactive liquid (A) (about 7 g.) was first collected. It gave a strong positive reaction with the fuchsine aldehyde reagent, but was not further examined. The second fraction (B) consisted of some 35 g. of greenish-yellow material, the rotation of which was $\alpha_{5461}^{22^\circ}$ (100 mm.) = + 8·4°. It gave a moderate fuchsine aldehyde reaction—possibly because it still contained some of fraction (A)—and reduced Fehling's solution; in direct contrast, in both respects, to the original ethyl tartrate. The succeeding fractions, which, since they all consisted of ethyl tartrate containing but a small proportion of an impurity boiling at only a slightly lower temperature than the ethyl tartrate itself, showed no appreciable temperature range, gave the following results for l = 100 mm. : (C), 25 g., greenish, $\alpha_{5461}^{17^\circ}$ + 10·5°; (D) 25 g., almost colourless, $\alpha_{5461}^{18\cdot7^\circ}$ + 11·55°; (E) 42 g., colourless, $\alpha_{5461}^{18\cdot2^\circ}$ + 11·4°. The second fraction (B) gradually lost most of its colour on standing for a month in a stoppered flask, but the colour returned again on heating. The colour was immediately destroyed by addition of a drop of water to 0·5 c.c. of the product.

At this point, Sir Gilbert Morgan having mentioned, in conversation, that glyoxal turns green on heating, we added to a sample of colourless ethyl tartrate a small quantity (1%) of glyoxal; when the solution was heated, a colour, similar to that which had been observed in our earlier experiments, developed, and faded again on cooling. The formation of glyoxal itself from ethyl tartrate by oxidation seemed unlikely, but the observation supported the idea, originally held, that the colouration might be due to a ketosuccinic ester. The experiment with glyoxal also gave some notion of the amount of impurity sufficient to cause the green colour in the ethyl tartrate, and also suggested some experiments on its recognition.

To ethyl tartrate containing 1% of glyoxal, absolute alcohol (3 vols.) was added, and then a solution in alcohol of 2 : 4-dinitrophenylhydrazine sulphate. This gave an orange precipitate which was practically insoluble in glacial acetic acid and did not melt below 280°.

With 2 : 4-dinitrophenylhydrazine, a portion of the fraction (B) also yielded a precipitate (1·1 g. from 4·84 g. of green ester), which, however, was lighter in colour than that due to glyoxal. Crystallised from acetic acid, it decomposed at 180—200°, and after five crystallisations from chloroform, formed small lemon-yellow needles, decomposing gradually above 180° [Found : C, 42·6; H, 3·25; N, 20·1. $\{C_6H_3(NO_2)_2\cdot NH\cdot N{:}C(CO_2Et)\cdot\}_2$ requires C, 42·7; H, 3·2; N, 19·9%]. The first crop of crystals contained also a small quantity of bright red crystals, which could not be isolated for further examination.

It seems very probable, therefore, that the substance present in the ethyl tartrate, to which the green colouration on heating is due, is ethyl diketosuccinate, although there is a possibility that, if ethyl hydroxyketosuccinate were the active agent, it might be oxidised, by the 2 : 4-dinitrophenylhydrazine, to diketosuccinic ester, which then could yield the *bis-2 : 4-dinitrophenylhydrazone*. This view appears to be corroborated by the experiments of Astin and Riley (J., 1934, 845), who oxidised ethyl tartrate by means of selenium dioxide and isolated ethyl hydroxyketosuccinate, which was found to form, not a mono-, but a bis-hydrazone with phenylhydrazine. This bis-hydrazone, on boiling with glacial acetic acid, as was observed by Anschütz and Parlatto (*Ber.*, 1892, **25**, 1979) gave the 4-phenylhydrazone of ethyl 4 : 5-diketo-1-phenyl-4 : 5-dihydropyrazole-3-carboxylate, m. p. 153·5°.

Our sample of "green" ethyl tartrate (B), with phenylhydrazine acetate in aqueous solution, gave a pasty yellow precipitate, which, on boiling with glacial acetic acid, and then dilution with water, yielded a substance, m. p. 153—154°, identical with that described by Anschütz and Parlatto (Found : N, 16·6. Calc. : N, 16·7%).

Astin and Riley do not refer to any green colour in their esters, but Astin, Moulds, and Riley (J., 1935, 902) mention a yellow colour produced by selenium dioxide oxidation of ethyl malate to ethyl diketosuccinate; ethyl tartrate was oxidised only to ethyl hydroxyketosuccinate. We obtained no green product on aerating ethyl malate in the same way that we had adopted with ethyl tartrate.

In corroboration of these results we found that, when a mixture of ethyl tartrate with a small quantity of ethyl diketosuccinate (Anschütz and Parlatto, *Ber.*, 1892, **25**, 1976) was heated, a green colour developed, which faded on cooling; and, on treatment with 2 : 4-dinitrophenylhydrazine, the mixture behaved in a manner similar to that of the " green " ethyl tartrate of fraction (B), yielding a hydrazone (Found : C, 42·55; H, 3·3; N, 19·7%). In addition, the pyrazole obtained with phenylhydrazine, as described above, from " green " ethyl tartrate, was identical (m. p. and mixed m. p.) with a synthetic specimen prepared from ethyl diketosuccinate and phenylhydrazine.

Experiments with Other Analogous Esters.—Methyl tartrate and *iso*butyl tartrate behaved like ethyl tartrate, but only a weakly coloured specimen could be obtained from the former, owing to decomposition.

In the case of *iso*butyl tartrate the colouration was concentrated as in the ethyl ester, but without the rod and disc; by some twelve aerations and distillations, 60 g. of *iso*butyl tartrate yielded 23 g. of moderately " green " ester. The concentration was not so effective as in the case of the ethyl ester; the colouration could be removed by crystallisation from benzene, and concentrated to some extent in the mother-liquors.

With an alcoholic solution of the aerated ester, 2 : 4-dinitrophenylhydrazine sulphate gave the yellow bis-2 : 4-dinitrophenylhydrazone of *iso*butyl diketosuccinate (Found : N, 18·4. Calc. for $C_{24}H_{26}O_{12}N_8$: N, 18·1%). It had no definite m. p., but decomposed about 180°.

5 G. of the " green " *iso*butyl ester were boiled for 15 minutes with 0·5 g. of phenylhydrazine acetate in glacial acetic acid. The orange-coloured solid (mainly *iso*butyl tartrate) obtained by precipitation with water was dried and crystallised from carbon disulphide. The mother-liquor, after removal of *iso*butyl tartrate, was evaporated, and the residue, after two recrystallisations from methylated spirit, yielded a few mg. of felted, orange needles, m. p. 127—128°, identical with a synthetic specimen of the 4-phenylhydrazone of *iso*butyl 4 : 5-diketo-1-phenyl-4 : 5-dihydropyrazole-3-carboxylate, prepared from *iso*butyl diketosuccinate, which, in turn, was obtained, by Anschütz and Parlatto's method (*loc. cit.*), from sodium dihydroxytartrate and *iso*butyl alcohol. The *iso*butyl diketosuccinate was a viscous red oil, b. p. 109—112°/3 mm. It was not analysed as such, since v. Auwers reported (*Ber.*, 1918, **51**, 1121) that the corresponding ethyl diketosuccinate could not be obtained pure by distillation. Its identity was, however, amply confirmed by the formation of the bisphenylhydrazone (Found : N, 18·1. Calc. : N, 18·1%) and the above-mentioned pyrazole (Found : C, 65·8; H, 5·6; N, 15·2. Calc. : C, 65·9; H, 5·5; N, 15·4%). With a little water, a colourless oil was obtained which ultimately yielded a white solid, m. p. 87—90° (from carbon disulphide). This, of which we had only a small quantity, gave analytical results approximating to those required for a monohydroxide (Found : C, 53·0; H, 7·0. Calc. : C, 52·1; H, 7·2%). When either this substance or the original *iso*butyl diketosuccinate was added to hot colourless *iso*butyl tartrate, the colouration of the " green " ester was exactly imitated.

The foregoing experiments appear to show that, when air is aspirated through hot ethyl tartrate, an easily volatile, optically inactive, aldehydic compound is produced (which was not further examined), along with some ethyl diketosuccinate (formed probably *via* the ethyl hydroxyketosuccinate); and that to this diketosuccinate is owing the appearance and disappearance of a greenish-yellow colour on heating and cooling respectively. The mechanism of the change of colour with heating and cooling remains, however, obscure, although there is some evidence in favour of its being due to hydration (Wahl, *Bull. Soc. chim.*, 1908, **3**, 24). With this view our observations are not inconsistent; since (1) the green colouration in ethyl tartrate disappeared immediately on addition of water, and (2), when the colourless solid obtained from *iso*butyl diketosuccinate and water was added to hot molten *iso*butyl tartrate, a green colour was produced.

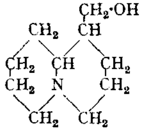
The authors express their thanks to the Carnegie Trustees for the Universities of Scotland for assistance towards the cost of this investigation, and one of them, in addition, for a Carnegie Scholarship.

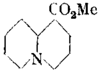
University of Glasgow. [*Received, April 28th, 1937.*]

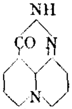
199. *The Lupin Alkaloids. Part XII. The Synthesis of* dl-*Lupinine and* dl-iso*Lupinine.*

By G. R. Clemo, W. McG. Morgan, and R. Raper.

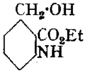
Karrer and his co-workers (*Helv. Chim. Acta*, 1928, **11**, 1062), on the basis of degradation evidence, advanced formula (I) for lupinine, and we have been engaged for some time on its synthesis. In Part V (J., 1931, 3190) we described work leading to the production of (II), and from this, by the Bouveault reaction, we obtained a substance from which, although it should have structure (I), we could not obtain *l*-lupinine. The substance (II), however, was obtained from methyl 1-keto-octahydropyridocoline-9-carboxylate by the Clemmensen reduction; but we have since shown (Part XI; J., 1936, 1429) that, whereas the Clemmensen reduction of 1-keto-octahydropyridocoline gives the B form of octahydropyridocoline, differing from the A form obtained from lupinine, the Wolff reduction gives the latter,


(I.)


(II.)


(III.)

and hence it appeared to be desirable to carry out the latter reduction on the 9-keto-ester in order to see if *dl*-lupinine could be obtained from the product. The reduction of quinolinic acid to the hexahydro-compound and the separation of this into its *cis*- and *trans*-forms through the nitrosoamines (Besthorn, *Ber.*, 1895, **28**, 3151) are tedious, and so the mixed stereoisomers were condensed with γ-bromobutyronitrile, and the product ring-closed, after hydrolysis and esterification, to methyl 1-keto-octahydropyridocoline-9-carboxylate (Part V; J., 1931, 3197). This compound on treatment with hydrazine hydrate gave the *pyridazine* derivative (III), but only in poor yield, and it was clear that this method could not be used in a satisfactory lupinine synthesis.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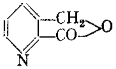
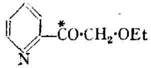

(V.)


(VI.)

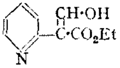
Attention was then turned to the preparation of 2-carbethoxy-3-piperidylcarbinol (IV), from which it was hoped to prepare *dl*-lupinine by the methods used in previous papers of this series for the production of the octahydropyridocoline ring system. We were, however, unable to reduce quinolinimide (Sucharda, *Ber.*, 1925, **58**, 1727) to quinolinide (V) by the methods which work well for phthalimide, and the method of Zincke (*Annalen*, 1896, **290**, 332) for the production of the unreduced form of (IV) is so long as to be unsatisfactory for our present purposes. Quinolinimide was also recovered unchanged from catalytic hydrogenation under the Adams–Shriner conditions.

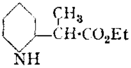
We then attempted to prepare 2-ω-ethoxyacetylpyridine (VI), into which we hoped to introduce a trimethylene chain at the carbon atom * by means of the Grignard reaction, but the Claisen condensation of ethyl picolinate with ethyl ethoxyacetate gave only a very small trace of condensation product. The *p*-toluenesulphonyl ester of the oxime of 2-acetylpyridine was treated with potassium ethoxide (compare Neber and Huh, *Annalen*, 1935, **515**, 292), and the crude hydrochloride of ω-aminoacetylpyridine so obtained converted by nitrous acid into the diazo-compound, but this, on boiling with methyl alcohol, gave only a red oil, analysis of whose derivatives suggested that it was impure ω-aminoacetylpyridine.

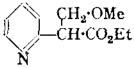
2-Acetylpyridine can be brominated to give the ω-*bromo*-derivative, but attempts to

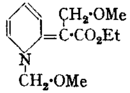
replace the bromine by the methoxyl or phenoxyl group gave red tars from which nothing definite could be isolated, and no reaction occurred with potassium phthalimide.

Meanwhile we made many attempts starting from ethyl 2-pyridylacetate. This condenses with ethyl formate to give the *hydroxymethylene* derivative (VII) in good yield. This crystalline compound is somewhat unstable, and, with picric and picrolonic acids, gives the salts of ethyl pyridylacetate. Unsuccessful attempts were made to methylate the hydroxyl group by means of methyl iodide and sulphate and diazomethane, and by successive treatments with phosphorus pentachloride and sodium methoxide, and it could not be benzoylated. Attempts to obtain quaternary salts with ethyl β-chloro-, -bromo-,


(VII.)

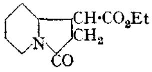

(VIII.)

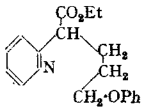

(IX.)

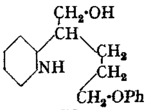

(X.)

and -iodo-propionates gave either (in the cold) no action, or, on warming, only 1-carbethoxy-4-keto-3-(2′-pyridyl)pyridocoline (Part X; J., 1936, 1026). Reduction of (VII) with sodium or aluminium amalgam was unsatisfactory, catalytic reduction with hydrogen and palladised charcoal did not affect the substance, and aluminium *iso*propoxide gave only the corresponding *isopropyl* ester. Catalytic reduction under the Adams-Shriner conditions gave an oil, which, treated with ethyl β-chloro- or -bromo-propionate, gave a condensation product from which two *picrolonates*, m. p.'s 136° and 115°, were obtained. If the picrolonate of the reduction product is very carefully fractionated from methyl alcohol, it is possible to obtain from it the picrolonate of ethyl pyridylacetate, a small amount of a *picrolonate*, m. p. 124°, not further investigated, and two *picrolonates* (C and D) of m. p.'s 209° and 185°. Analyses of these and the bases recovered from them showed that the latter were the two stereoisomeric forms of ethyl piperidyl-2-α-propionate (VIII), the catalytic reduction having converted the hydroxymethylene group into methyl. Condensation of the base from C with ethyl β-chloropropionate yielded an oil which gave the picrolonate, m. p. 115°, and similarly we obtained the picrolonate, m. p. 136°, from D. The Dieckmann reaction, carried out with either the mixed or the separated *ethyl piperidyl-1-β-propionate-2-α-propionates*, gave the same 2-keto-1-methyloctahydropyridocoline, but, as this could not be reduced by the Clemmensen method, and it could not lead to *dl*-lupinine, no further work on its reduction was carried out.

We then condensed ethyl 2-pyridylacetate with chloromethyl ether, but analysis of the product indicated it was a mixture of (IX) and (X). The condensation of ethyl pyridylacetate with ethyl chloroacetate yields *ethyl 2-pyridylsuccinate*, which is easily reduced to the piperidyl ester; this, however, cannot be purified, as, on distillation, it cyclises to *ethyl 3-keto-octahydropyrrocoline-1-carboxylate* (XI). Attempts to condense ethyl 2-piperidylsuccinate with ethyl β-bromopropionate, with the idea of ring-closing the condensation product by the Dieckmann reaction to ethyl 2-keto-octahydropyridocoline-1-acetate and thence obtaining structure (I) by a Curtius degradation, also failed, as no condensation on the imino-group could be effected.

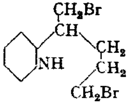
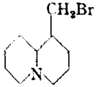

(XI.)


(XII.)


(XIII.)

Success in the synthesis of structure (I) was finally achieved by condensing ethyl pyridyl-2-acetate with γ-phenoxy-*n*-propyl bromide, yielding (XII), catalytic reduction, followed by Bouveault reduction, of which gave the *carbinol* (XIII). When this was treated with fuming hydrobromic acid, a mixture was obtained consisting mainly of (XIV).

In the course of working up this mixture the dibromo-compound cyclised, yielding the bromo-base (XV) together with a little unbrominated product. The whole was therefore

(XIV.)   (XV.)

treated with phosphorus pentabromide; the resulting *bromo-base* (XV) gave two *picrolonates* (J), m. p. 202°, and (K), m. p. 169°, by means of which it was separated into its two racemic forms. In Part VI (J., 1932, 2959) we showed that ring-closures of the type (XIV) ⟶ (XV) lead exclusively to the A form of octahydropyridocoline, and thus the occurrence of only two racemates is accounted for satisfactorily. The two forms, L and M, of *dl*-bromolupinane (XV) recovered from J and K respectively were hydrolysed by refluxing with sodium acetate solution, giving the two racemic forms of 1-*octahydropyridocolylcarbinol* (I), N and O. One of these should be *dl*-lupinine and the other *dl-iso*lupinine (Winterfeld and Holschneider, *Ber.*, 1931, **64**, 137; Schöpf, Schmidt, and Braun, *ibid.*, p. 683, name this base *epi*lupinine), but the amounts available so far have been too small for resolution, and work is in hand to prepare sufficient quantities of the two racemic bases to allow this to be effected.

Experimental.

3-*Ketodecahydro*peri*pyridazopyridocoline* (III).—Methyl 1-keto-octahydropyridocoline-9-carboxylate (0·2 g.) and hydrazine hydrate (0·3 g.) were mixed; heat was developed, and the *pyridazine* (III) (0·1 g.), m. p. 125—135°, deposited. Recrystallised from water, this had m. p. 137° (Found: C, 57·2; H, 8·0. $C_{10}H_{15}ON_3,H_2O$ requires C, 56·9; H, 8·0%).

2-ω-*Bromoacetylpyridine*.—2-Acetylpyridine (2 g.) in benzene (20 c.c.) and glacial acetic acid (5 c.c.) was gradually treated with bromine (2·65 g.) in benzene (12·6 c.c.). The colourless precipitate (3·65 g., decomp. 226°) was collected and treated with an excess of saturated potassium carbonate solution, and the liberated oil taken up in ether, dried, and distilled, giving acetylpyridine (0·15 g.), b. p. 37—40°/1 mm., identified as the picrate, m. p. 136° (given as 131° in Beilstein's "Organische Chemie"), and ω-*bromoacetylpyridine* (0·9 g.), b. p. 88°/1 mm. (Found: C, 42·5; H, 3·3. C_7H_6ONBr requires C, 42·0; H, 3·0%). The base (0·6 g.) was heated for 2 hours with potassium permanganate (1 g.) in water (15 c.c.) and concentrated sulphuric acid (5 c.c.), and the whole basified (sodium carbonate) and evaporated to dryness. The residue was mixed with soda-lime and distilled, the distillate dissolved in concentrated hydrochloric acid and evaporated to dryness, and the residue basified; the pyridine obtained was identified as the picrate, m. p. and mixed m. p. 163°.

Ethyl Hydroxymethylene-2-pyridylacetate (VII).—Potassium (2 g.) was dissolved in dry ether (50 c.c.) and alcohol (7·2 c.c.), and ethyl 2-pyridylacetate (8 g.) and ethyl formate (4 g.) added with ice-cooling. After 18 hours water was added, the ethereal layer separated, and the aqueous layer acidified to Congo-red, basified (potassium carbonate), and ether-extracted. The ether was removed, and the residue recrystallised from light petroleum, giving a felt of pale yellow needles (6 g.), m. p. 97° (Found: C, 62·0; H, 5·5. $C_{10}H_{11}O_3N$ requires C, 62·2; H, 5·7%). The substance gives an intense red coloration with ferric chloride. The *hydroxymethylene* compound (1·9 g.), aluminium *iso*propoxide (0·15 g.), and *iso*propyl alcohol (2 c.c.) were slowly distilled through a column. No acetone distilled (negative reactions with sodium nitroprusside and *p*-nitrophenylhydrazine). The residue was concentrated, taken up in dilute hydrochloric acid, basified (potassium carbonate), and ether-extracted. On removal of the ether and recrystallisation of the residue from light petroleum, unchanged material (0·8 g., m. p. 96° alone or mixed) was obtained. The concentrated mother-liquor deposited an oil, which solidified after distillation. Recrystallised from light petroleum, it melted at 78° alone or mixed with authentic iso*propyl hydroxymethylene-2-pyridylacetate* prepared in the same way as the ethyl ester (Found: C, 63·4; H, 6·6. $C_{11}H_{13}O_3N$ requires C, 63·7; H, 6·3%).

*iso*Propyl 2-pyridylacetate gives a *picrolonate*, m. p. 187° (Found: C, 54·5; H, 5·1. $C_{10}H_{13}O_2N,C_{10}H_8O_5N_4$ requires C, 54·2; H, 4·75%).

Ethyl 2-Piperidyl-α-propionate.—Ethyl hydroxymethylene-2-pyridylacetate (8·5 g.) in

glacial acetic acid (60 c.c.) was shaken with platinum oxide (0·5 g.) in hydrogen at 100 lb./sq. in. for 40 hours; the product, worked up in the usual way, yielded an oil (5 g.), b. p. 80°/1 mm. Its picrolonate, prepared in ethyl alcohol and recrystallised from methyl alcohol, aided by hand-picking, gave (a) ethyl pyridylacetate picrolonate, m. p. 157° alone or mixed with an authentic specimen, (b) a small amount of a *picrolonate*, m. p. 124°, probably of ethyl pyridyl-α-propionate (Found: C, 54·2; H, 4·8. $C_{10}H_{13}O_2N,C_{10}H_8O_5N_4$ requires C, 54·2; H, 4·8%), (c) *picrolonate C*, m. p. 209° (Found: C, 53·4; H, 6·1%), and (d) *picrolonate D*, m. p. 185° (Found: C, 53·8; H, 6·25. $C_{10}H_{19}O_2N,C_{10}H_8O_5N_4$ requires C, 53·4; H, 6·0%).

Ethyl 1-*Piperidyl*-β-*propionate*-2-α-*propionates E and F*.—The base (0·5 g., b. p. 80°/1 mm.) recovered from picrolonate C (1·6 g.) was heated with ethyl β-chloropropionate (0·9 g.) and anhydrous potassium carbonate (1·4 g.) in a sealed tube for 5 hours in the water-bath, water and excess of potassium carbonate added, and the oil taken up in ether. The basic portion was shaken out in dilute hydrochloric acid, liberated (50% potassium carbonate), ether-extracted, dried, and distilled, giving some unaltered base and an oil (0·25 g.), b. p. 145—150°/1 mm., whose *picrolonate G* had m. p. 115° (Found: C, 54·8; H, 6·8. $C_{15}H_{27}O_4N,C_{10}H_8O_5N_4$ requires C, 54·6; H, 6·4%). *Ethyl piperidyl*-1-β-*propionate*-2-α-*propionate E* recovered from this picrolonate had b. p. 136—138°/1 mm. (Found: C, 63·1; H, 9·6; N, 4·9. $C_{15}H_{27}O_4N$ requires C, 63·2; H, 9·5; N, 4·9%).

The base recovered from picrolonate D, similarly treated with ethyl β-chloropropionate, gave an oil, b. p. 145—150°/1 mm. This gave *picrolonate H*, m. p. 136° (Found: C, 54·2; H, 6·5. $C_{15}H_{27}O_4N,C_{10}H_8O_5N_4$ requires C, 54·6; H, 6·4%), and the *ethyl piperidyl*-1-β-*propionate*-2-α-*propionate F* recovered from it had b. p. 145°/1 mm. (Found: C, 62·9; H, 9·6. $C_{15}H_{27}O_4N$ requires C, 63·2; H, 9·6%). The esters E and F are more readily obtained by treating the mixed isomers of ethyl 2-piperidyl-α-propionate with ethyl β-chloropropionate as above; picrolonates G and H are then readily separated by fractional crystallisation from alcohol of the mixture obtained from the crude condensation product.

2-*Keto*-1-*methyloctahydropyridocoline*.—The mixture of esters E and F obtained as above (2·5 g.) was added to powdered potassium (0·9 g.) in toluene (20 c.c.), and the whole heated for 6 hours on the water-bath. Alcohol was added to dissolve unused potassium, then water (10 c.c.) and concentrated hydrochloric acid (30 c.c.), and the whole heated for a further 18 hours and evaporated to dryness. The residue was basified (50% potassium hydroxide) and ether-extracted, and the extract distilled, giving 2-keto-1-methyloctahydropyridocoline (0·6 g.) as a colourless oil, b. p. 78—80°/1 mm. The homogeneous *picrate* had m. p. 202° (from alcohol) (Found: C, 48·7; H, 5·0. $C_{10}H_{17}ON,C_6H_3O_7N_3$ requires C, 48·5; H, 5·05%). The separated base E gave the same result [picrate (m. p. 202° alone or mixed) and a *picrolonate*, m. p. 209° (Found: C, 55·1; H, 6·1. $C_{10}H_{17}ON,C_{10}H_8O_5N_4$ requires C, 55·6; H, 5·8%)].

Ethyl 2-Pyridylsuccinate.—Ethyl 2-pyridylacetate (12·8 g.) was added to an ice-cold solution of potassium (3·2 g.) in alcohol (40 c.c.); after ½ hour ethyl chloroacetate (9·6 g.) was added, and the whole left overnight. The alcohol was removed, water added, and the solution extracted with ether. The basic part was shaken out with dilute hydrochloric acid, liberated (potassium carbonate), and ether-extracted. Distillation gave unchanged ethyl pyridylacetate (6·75 g.), b. p. 93—110°/1 mm., identified as picrate and picrolonate, and *ethyl 2-pyridylsuccinate* (3·4 g.), as a pale yellow oil, b. p. 143—147°/1 mm. (Found: C, 62·2; H, 6·9. $C_{13}H_{17}O_4N$ requires C, 62·1; H, 6·8%). The *picrolonate* formed rosettes of yellow prisms from alcohol, m. p. 95° (Found: C, 53·75; H, 5·3. $C_{13}H_{17}O_4N,C_{10}H_8O_5N_4$ requires C, 53·6; H, 4·85%).

Ethyl 3-Keto-octahydropyrrocoline-1-carboxylate.—Ethyl 2-pyridylsuccinate (3·4 g.) in glacial acetic acid (20 c.c.) was shaken with platinum oxide (0·1 g.) in hydrogen at 100 lb./sq. in. for 48 hours. On being worked up in the usual way and distilled, the product underwent considerable decomposition, yielding *ethyl 3-keto-octahydropyrrocoline-1-carboxylate* (2·3 g.), b. p. 148—150°/1 mm. (Found: C, 62·3; H, 8·2. $C_{11}H_{17}O_3N$ requires C, 62·6; H, 8·1%).

Ethyl 2-Piperidylsuccinate.—After reduction of ethyl 2-pyridylsuccinate by the above method, the acetic acid was removed at 30—35° in a vacuum. After basification (potassium carbonate) and ether-extraction, the ether was evaporated at room temperature, leaving an oil (2·8 g.) which appeared to be ethyl 2-piperidylsuccinate, as it gave a *picrolonate*, m. p. 166° (Found: C, 52·6; H, 5·7. $C_{13}H_{23}O_4N,C_{10}H_8O_5N_4$ requires C, 53·0; H, 5·95%). This ester did not react in the cold with ethyl β-chloro- or -iodo-propionate or with β-cyanoethyl *p*-toluenesulphonate, and, on warming with any of these, immediate cyclisation took place.

Ethyl δ-*Phenoxy*-α-2-*pyridyl*-n-*valerate* (XII).—Ethyl 2-pyridylacetate (8·2 g.) was added to potassium powder (2·0 g.) suspended in dry ether (100 c.c.). After 18 hours γ-phenoxy-*n*-propyl bromide (11 g.) was added, and the whole refluxed for 6 hours. Water was added to dissolve

potassium bromide, the ethereal layer separated, and the aqueous layer extracted with ether. The basic part was shaken out (dilute hydrochloric acid), liberated (potassium carbonate), taken up in ether, dried, and distilled, giving *ethyl δ-phenoxy-α-2-pyridyl*-n-*valerate* (5 g.) as a golden-yellow oil, b. p. 205—207°/1 mm. (Found: C, 72·2; H, 7·3. $C_{18}H_{21}O_3N$ requires C, 72·2; H, 7·0%).

Ethyl δ-Phenoxy-α-2-piperidyl-n-*valerate*.—The above ester (5·0 g.) was shaken in glacial acetic acid (30 c.c.) with platinum oxide (0·2 g.) in hydrogen at 100 lb./sq. in for 18 hours. On working up, the *piperidyl* ester was obtained as a thick colourless oil (4 g.), b. p. 190—192°/1 mm. (Found: C, 70·6; H, 8·5; N, 5·0. $C_{18}H_{27}O_3N$ requires C, 70·8; H, 8·8; N, 4·6%). The ester gave the Liebermann reaction.

ε-Phenoxy-β-2-piperidyl-n-*amyl Alcohol* (XIII).—The above ester (12 g.) in alcohol (150 c.c.) was added to sodium (18 g.) at 180°, followed by enough alcohol to dissolve the sodium. The solution was acidified (concentrated hydrochloric acid) and evaporated, the residue basified (50% aqueous potassium hydroxide), and the liberated oil extracted and distilled, giving the *carbinol* as a very thick, pale yellow oil (6 g.), b. p. 195—200°/1 mm. (Found: C, 72·9, 73·3; H, 9·25, 9·6; N, 5·6. $C_{16}H_{25}O_2N$ requires C, 73·0; H, 9·5; N, 5·3%).

1-*Bromomethyloctahydropyridocoline* (XV).—The above carbinol (12·5 g.) in hydrobromic acid (100 c.c., *d* 1·65) was kept for 18 hours and then refluxed for 7 hours, and the solution evaporated. The residue was basified (30% potassium hydroxide solution) and extracted with ether, and the ethereal extract, after standing for 18 hours, was again shaken with 30% potassium hydroxide solution, dried, and fractionated. The crude distillate, in benzene (15 c.c.), was refluxed for 1½ hours with phosphorus pentabromide (7 g.), the whole cooled, and ice added, followed by an excess of potassium hydroxide solution (20%). The benzene layer was separated, and the aqueous layer extracted twice with benzene. The united dried benzene extracts were evaporated, and the residue distilled, yielding an oil (6·6 g.), b. p. 110°/1 mm. This was converted into picrolonate (12 g.), and the latter fractionally crystallised from alcohol, giving *picrolonate J* (5·3 g.), m. p. 202° (Found: C, 48·5, 48·3; H, 5·6, 5·6. $C_{10}H_{18}NBr,C_{10}H_8O_5N_4$ requires C, 48·4; H, 5·25%), and *picrolonate K* (4·3 g.), m. p. 169° (Found: C, 48·4, 48·2; H, 5·5, 5·3%).

The *base L* recovered from picrolonate J (5·3 g.) had b. p. 107°/1 mm. (1·8 g.) (Found: C, 51·3; H, 7·7. $C_{10}H_{18}NBr$ requires C, 51·7; H, 7·8%), and gave a *methiodide*, m. p. 216° (Found: C, 35·1; H, 5·75. $C_{10}H_{18}NBr,CH_3I$ requires C, 35·3; H, 5·6%), and *picrate*, m. p. 135° (Found: C, 41·5; H, 4·9. $C_{10}H_{18}NBr,C_6H_3O_7N_3$ requires C, 41·6; H, 4·55%).

The *base M* was recovered from picrolonate K as an oil (2 g.), b. p. 107°/1 mm. (Found: C, 51·2; H, 7·6); it gave a *picrate*, m. p. 144° (Found: C, 41·3; H, 4·9%), and a methiodide, m. p. 186°.

1-*Octahydropyridocolylcarbinols N and O*.—The bromo-base L (1·7 g.) was refluxed with sodium acetate (7 g.) in water (15 c.c.) for 10 hours, and the solution acidified to Congo-red (hydrochloric acid) and evaporated to dryness. The residue was basified (potassium carbonate) and extracted with ether, and the extract fractionated, giving 1-*octahydropyridocolylcarbinol N* (0·42 g.), b. p. 107°/1 mm. This solidified, and formed prisms, m. p. 59°, from light petroleum (b. p. 40—60°) (Found: C, 71·3; H, 11·3. $C_{10}H_{19}ON$ requires C, 71·0; H, 11·2%). The *methiodide* had m. p. 303° (decomp.) (Found: C, 42·4; H, 7·3. $C_{10}H_{19}ON,CH_3I$ requires C, 42·4; H, 7·1%), the *picrolonate*, m. p. 203° (Found: C, 55·7; H, 6·1. $C_{10}H_{19}ON,C_{10}H_8O_5N_4$ requires C, 55·4; H, 6·2%), and the *picrate*, m. p. 127° (Found: C, 48·6; H, 5·6. $C_{10}H_{19}ON,C_6H_3O_7N_3$ requires C, 48·2; H, 5·5%).

In a similar manner the bromo-base M gave the *carbinol O*, b. p. 122°/1 mm., m. p. 81° (Found: C, 70·8; H, 11·7%). This formed a *picrate*, m. p. 139° (Found: C, 48·0; H, 5·9%), *picrolonate*, m. p. 225° (Found: C, 55·5; H, 6·4%), and *methiodide*, m. p. 248° (Found: C, 42·6; H, 7·2%).

We thank the Royal Society for a grant; one of us (W. McG. M.) also thanks the Council of Armstrong College for a Scholarship, and the Department of Scientific and Industrial Research for a maintenance grant.

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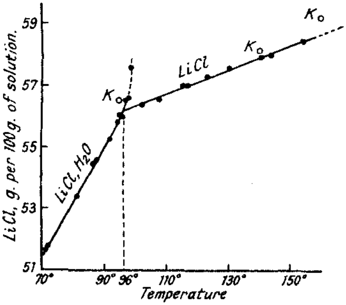
200. *The Solubility of Lithium Chloride in Water between 70° and 160°.*

By J. Newton Friend, Reginald W. Hale, and Samuel E. A. Ryder.

The solubilities of the two hydrates of lithium chloride in water have already been determined by usual methods (Friend and Colley, J., 1931, 3148) between 0° and 88°. Above 96° the stable solid phase consists of the anhydrous salt, but attempts to determine its solubility, by using an oil-bath and an apparatus similar to that of Walton and Judd (*J. Amer. Chem. Soc.*, 1911, **33**, 1036), yielded irregular results. This was apparently due to the great stability of $LiCl,H_2O$ in the metastable state above the transition temperature. It was decided, therefore, to adopt the synthetic method.

Mixtures of anhydrous salt and water were heated in sealed tubes in an oil-bath with repeated shaking until the solid phase disappeared, the mean temperature after repeated trials being evaluated. The anhydrous salt crystallised on cooling as flakes, like boric acid, which floated in the viscous solution, and their glistening appearance enabled the moment of their disappearance on re-warming to be noted with relative ease. Experiments at temperatures below 96° showed that this synthetic method gave results identical within the error of experiment with the ordinary method.



K = *Kremers*, loc. cit.

The concentration of lithium chloride was determined either, as before, by evaporation of an aliquot portion in a platinum dish, followed by momentary heating to incipient fusion to render the salt anhydrous, or by titration with silver nitrate solution. The two methods gave closely concordant results.

Kremers (*Pogg. Ann.*, 1856, **99**, 25) gave the solubilities of lithium chloride at 65°, 95°, 140°, and 160°. Since then no systematic study of the subject appears to have been published. His temperature intervals are too large to enable even an approximate value for the transition temperature of $LiCl,H_2O \rightleftharpoons LiCl$ to be estimated. Bogorodsky (*J. Russ. Phys. Chem. Soc.*, 1893, **25**, 316) gave 98° for this point.

In the following table *S* represents the solubility as g. of anhydrous lithium chloride per 100 g. of solution.

Temp.	*S*.	Solid phase.*	Ref.	Temp.	*S*.	Solid phase.*	Ref.	Temp.	*S*.	Solid phase.*	Ref.
71·5°	51·61	A		95·3°	56·01	A		117·0°	57·00	C	
72·0	51·71	,,	F. & C.	95·5	55·99	,,		123·0	57·28	,,	
81·6	53·37	,,	,,	96·2	56·57	B		130·5	57·58	,,	
87·0	54·46	,,		97·1	56·60	,,		140	58·1	,,	K.
88·0	54·54	,,	F. & C.	98·2	57·55	,,		140·5	57·90	,,	
92·0	55·27	,,		101·8	56·40	C		143·6	57·98	,,	
94·6	55·84	,,		107·6	56·52	,,		154·0	58·46	,,	
95·0	56·5	,,	K.	115·4	56·95	,,		160	59·2	,,	K.

* A = $LiCl,H_2O$; B = Metastable $LiCl,H_2O$; C = LiCl.

References.—F. & C. = Friend and Colley (*loc. cit.*); K = Kremers (*loc. cit.*).

The foregoing results are shown in the figure. The transition temperature $LiCl,H_2O \rightleftharpoons LiCl$ is approximately 96°. The solubility of the anhydrous salt is a linear function of the temperature like that of sodium chloride, but unlike that of potassium chloride. Kremers' results are, in general, too high.

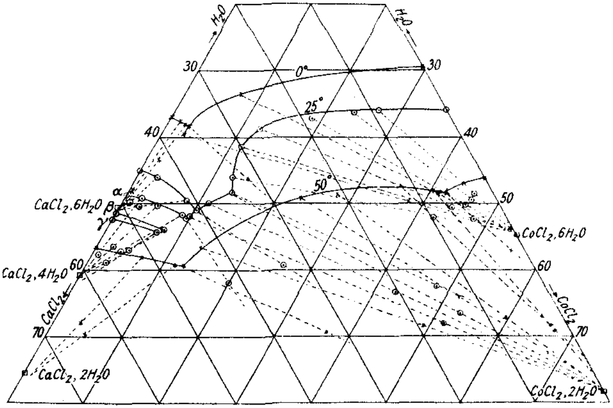
The Technical College, Birmingham. [*Received, May 1st, 1937.*]

201. *The Three-component Systems composed of Cobalt Chloride and Water with either Calcium, Strontium, or Thorium Chloride.*

By Henry Bassett, Horace F. Gordon, and Joseph H. Henshall.

A number of salts when added to solutions of cobalt chloride tend to turn these blue. Solid blue double salts have been isolated from such solutions in only a few cases, however. They have been obtained with magnesium chloride (Bassett and Croucher, J., 1930, 1784), lithium chloride (Bassett and Sanderson, J., 1932, 1855), and with rubidium and cæsium chlorides (Foote, *Amer. J. Sci.*, 1927, **13**, 158).

In the hope of adding to this number, the cobalt chloride systems containing either calcium, strontium, or thorium chloride have been examined, since all of these salts favour the blue condition. The results obtained are recorded in the tables and shown graphically for the calcium system. No double salts have been found, nor is there any indication of any



solid-solution formation. The system $CoCl_2$–$CaCl_2$–H_2O has been examined at 25° by Benrath (*Z. anorg. Chem.*, 1927, **163**, 396) whose results do not agree very well with ours. The stable region of $CoCl_2,2H_2O$ was missed and included in that of $CoCl_2,6H_2O$ because no proper examination or analysis of the solid phases was made. We find at 0° only the solid phases $CoCl_2,6H_2O$ and $CaCl_2,6H_2O$, and at 50° the three phases $CoCl_2,6H_2O$, $CoCl_2,2H_2O$, and $CaCl_2,2H_2O$. At 25°, in addition to $CoCl_2,6H_2O$, $CoCl_2,2H_2O$, and $CaCl_2,6H_2O$, which have stable fields of existence, we have been able to trace the solubility curves for the three forms of $CaCl_2,4H_2O$, all metastable at 25°; $CaCl_2,2H_2O$ was also found at this temperature but was too unstable for its solubility to be measured. The solubility curve evidently lay in the position to be expected, approximately parallel to the curves for the tetrahydrate in the region of still lower water content. Inoculation with the appropriate solid was employed in tracing the curves of metastable compounds.

The system $CoCl_2$–$SrCl_2$–H_2O is very simple. It has been examined at 25°, where the two hexahydrates alone occur, and at 80°, where the two dihydrates are the only solid phases. The system was examined at 25° by Benrath (*loc. cit.*) whose results do not differ much from ours.

In the system $CoCl_2$–$ThCl_4$–H_2O at 25° there is a large region of $CoCl_2,6H_2O$ and a small one of $ThCl_4,8H_2O$. The solubility of the latter salt was determined also at 0°, and so was the position of the point of intersection of the solubility curves of the two chlorides, the two

solid phases being identified by means of the petrological microscope. No evidence was found for the existence of other solid phases at 0°. Various hydrates of thorium chloride have been reported in the literature but they have not been examined systematically in the light of the phase rule. Cleve (*Bihang. Svensk. Akad. Handl.*, 1874, **2**, 6, 10; *Bull. Soc. chim.*, 1874, **21**, 116) showed that $ThCl_4,8H_2O$ is formed at the ordinary temperature by evaporation of aqueous solutions. We find that the crystals are orthorhombic and positive with an optic axial angle of about 10°.

We have been able to characterise the three forms of $CaCl_2,4H_2O$ more fully than was done by Bassett *et alios* (J., 1933, 151). The α-form is triclinic and negative with an optic axial angle of about 30°. It forms crystals having a "granular" appearance. The β-form is orthorhombic and negative with an optic axial angle of about 5°. The crystals are often rectangular and are somewhat elongated in the direction of slow vibration. The γ-form is more difficult to define owing to its habit of crystallising in large, six-sided plates. These show straight extinction and elongation in the direction of slow vibration, and their general shape and angles are similar to those of one aspect of the much smaller crystals of the β-form. The interference figure shown by the large plates of the γ-chloride is a diffuse cross moving rapidly out of the field as the crystal is rotated. It is visible for less than 10° rotation of the stage. The interference figure shown by the similar small plates of the β-tetrahydrate is a single brush, invisible in the 45° position. It is probable that the crystals of the γ-form are orthorhombic but they certainly differ from the orthorhombic β-form.

During the crystallographic examinations it was found that the β-form was produced almost invariably if plates of the γ-form were crushed with a glass rod in the equilibrium solution. Previously the formation of the β-form had appeared to be somewhat fortuitous.

EXPERIMENTAL.

Iron- and nickel-free cobalt chloride was used. The thorium chloride was anhydrous material converted into octahydrate by crystallisation from water. Thorium and chlorine were shown to be present in the correct ratio.

$CoCl_2$–$CaCl_2$–H_2O.

Solution.		Moist solid.			Solution.		Moist solid.		
$CoCl_2$, %.	$CaCl_2$, %.	$CoCl_2$, %.	$CaCl_2$, %.	Solid phase.	$CoCl_2$, %.	$CaCl_2$, %.	$CoCl_2$, %.	$CaCl_2$, %.	Solid phase.
				At 0°.					
29·50	—	—	—	a	2·36	35·82	1·59	41·83	c
7·22	26·42	41·07	7·37	a	1·64	36·25	0·49	47·82	c
2·82	36·77	37·69	11·94	a	—	37·00	—	—	c
2·85	35·48	14·53	31·46	a, c					
				At 25°.					
35·87	—	—	—	a	8·34	41·13	2·49	47·91	c
26·88	9·08	45·99	2·39	a	2·77	43·37	0·86	48·96	c
23·66	12·61	45·92	3·33	a	—	45·05	—	—	c
18·50	18·66	45·62	4·50	a	m 9·51	42·53	20·03	41·84	b, d
12·44	26·10	44·05	6·35	a	m 8·76	42·91	3·56	53·60	d
11·39	29·92	47·79	4·62	a	m 4·92	45·27	2·14	54·29	d
12·52	33·46	42·17	9·84	a	m 2·14	46·94	0·78	56·79	d
13·51	34·83	48·07	14·25	a, b	mB —	48·85	—	—	d
13·64	34·90	53·15	13·42	b	m 7·56	46·27	2·33	56·55	e
11·43	38·54	42·94	20·32	b	mB —	51·30	—	—	e
m 9·75	41·99	51·83	16·22	b	m 6·92	47·24	4·42	52·52	f
10·36	40·63	25·71	33·47	b, c	mB —	52·13	—	—	f
				At 50°.					
46·00	—	—	—	a	23·24	25·98	51·63	12·42	b
43·50	3·34	53·54	0·26	a	13·72	42·85	49·23	19·40	b
41·92	6·31	55·30	1·92	a, b	12·79	46·63	36·60	32·74	b, g
40·22	7·87	67·10	1·94	b	11·55	47·74	5·00	64·60	g
35·41	11·88	66·08	2·21	b	6·75	51·43	3·64	64·34	g
27·67	20·87	59·53	7·70	b	—	56·70	—	—	g

m = Metastable; B = Bassett *et al.* (J., 1933, 151); a = $CoCl_2,6H_2O$; b = $CoCl_2,2H_2O$; c = $CaCl_2,6H_2O$; d = α-$CaCl_2,4H_2O$; e = β-$CaCl_2,4H_2O$; f = γ-$CaCl_2,4H_2O$; g = $CaCl_2,2H_2O$.

$CoCl_2$–$SrCl_2$–H_2O.

Solution.		Moist solid.			Solution.		Moist solid.		
$CoCl_2$, %.	$SrCl_2$, %.	$CoCl_2$, %.	$SrCl_2$, %.	Solid phase.	$CoCl_2$, %.	$SrCl_2$, %.	$CoCl_2$, %.	$SrCl_2$, %.	Solid phase.
		At 25°.					At 50°.		
35·87	—	—	—	a	49·50	—	—	—	c
32·57	4·28	50·86	0·22	a	42·16	10·71	69·93	1·98	c
29·21	9·00	53·05	0·16	a	41·02	12·25	75·00	0·04	c
26·90	12·19	30·13	24·65	a, b	31·98	22·16	37·78	32·32	c, d
26·57	12·31	35·94	14·97	a, b	33·77	22·30	61·18	9·31	c, d
24·55	13·69	8·20	44·12	b	24·45	29·24	7·65	67·50	d
24·17	14·50	3·54	53·13	b	18·05	34·12	7·83	63·06	d
10·83	24·93	1·46	55·63	b	—	47·50	—	—	d
—	35·07	—	—	b					

a = $CoCl_2,6H_2O$; b = $SrCl_2,6H_2O$; c = $CoCl_2,2H_2O$; d = $SrCl_2,2H_2O$.

$CoCl_2$–$ThCl_4$–H_2O.

	Solution.		Moist solid.				Solution.		Moist solid.		
	$CoCl_2$, %.	$ThCl_4$, %.	$CoCl_2$, %.	$ThCl_4$, %.	Solid phase.		$CoCl_2$, %.	$ThCl_4$, %.	$CoCl_2$, %.	$ThCl_4$, %.	Solid phase.
					At 0°.						
	0·55	55·20	24·40	33·16	a, b	B	—	55·61	—	—	b
A	—	55·75	—	—	b						
					At 25°.						
	35·87	—	—	—	a		4·21	54·25	22·93	38·04	a, b
	22·47	18·50	43·31	6·84	a		3·34	55·17	0·04	67·80	b
	17·34	26·26	44·63	7·25	a	C	1·97	56·25	0·33	68·11	b
	7·85	42·46	46·62	7·36	a		—	58·00	—	—	b

A, by Th estimation; B, by Cl estimation; C by estimation of Cl and Co, the latter after separation of Th; a = $CoCl_2,6H_2O$; b = $ThCl_4,8H_2O$.

The cobalt–calcium and cobalt–strontium mixtures were analysed by determining cobalt as Co_3O_4, after separation with α-nitroso-β-naphthol, and total chloride. Direct determination of calcium and strontium was less satisfactory, as it involved previous separation of cobalt as sulphide. Determination of strontium as sulphate in presence of cobalt gave high results owing to contamination with cobalt sulphate.

Thorium and total chloride were determined in the analyses of the cobalt–thorium mixtures, as it was found that α-nitroso-β-naphthol failed to separate the two metals. The solution taken for analysis was diluted to 150 c.c. and precipitated boiling with ammonia in presence of ammonium chloride. After being washed once with hot water, the precipitate was redissolved in hydrochloric acid and reprecipitated. These operations were repeated, sometimes six times, until a perfectly white precipitate free from cobalt was obtained. The thoria should be ignited over the blowpipe and weighed without undue delay, as it is hygroscopic.

THE UNIVERSITY, READING. [*Received, May 4th, 1937.*]

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202. *The Absorption Spectrum of Solid Anhydrous Cobalt Chloride.*

By O. RHYS HOWELL and ALBERT JACKSON.

As the result of a study of the absorption spectra of a number of cobalt pigments obtained by replacing other metallic atoms by cobalt in compounds of known crystal structure, the theory was advanced (Hill and Howell, *Phil. Mag.*, 1924, **48**, 833) that the colour of the cobaltous compounds, both in the solid state and in solution, is determined by the number of atoms or groups surrounding the cobalt atom: with four, the colour is blue; with six, it is red.

Strong evidence for the correctness of this view has been forthcoming from the subsequent determination of the crystal structure of some cobaltous compounds and of other compounds from which cobalt pigments have been derived (see *Ann. Reports*, 1927, **24**, 288); from the change in density and viscosity (Howell, J., 1927, 158), refractive index

and surface tension (*idem, ibid.*, p. 2039), and electrical conductivity (*idem, ibid.*, p. 2843) accompanying the change of colour of aqueous cobalt chloride solution on addition of hydrochloric acid; from the spectroscopic study of the change of colour of aqueous cobalt chloride solution on addition of hydrochloric acid (Howell and Jackson, *Proc. Roy. Soc.*, 1933, *A*, **142**, 587), of magnesium chloride (*idem*, J., 1936, 1268), or of potassium thiocyanate (*idem*, this vol., p. 621); and from the change in physical properties (Howell, J., 1929, 162) and in the absorption spectrum (Howell and Jackson, *Proc. Roy. Soc.*, 1936, *A*, **155**, 33) of aqueous solutions of cobalt chloride and hydrochloric acid with change of temperature.

There has appeared, however, one important fact in apparent opposition to the simple colour rule. It was shown (Ferrari, Celeri, and Giorgi, *Rend. R. Accad. Lincei*, 1929, **9**, 782), from *X*-ray examination by the powder method, that the chlorides of cobalt, cadmium, magnesium, iron, and nickel are all isomorphous. Subsequently, *X*-ray examination of a single crystal of cadmium chloride (Pauling and Hoard, *Z. Krist.*, 1930, **74**, 546) established that its crystal structure is of the layer type with each cadmium ion within a group of six chlorine ions. It follows that anhydrous cobalt chloride has the same type of structure.

The characteristics of salts possessing a layer structure are generally intermediate between those having a molecular and those having an ionic lattice. The layer structure of anhydrous cobalt chloride therefore explains its comparatively ready volatility and its solubility in organic solvents; also the fact that on sublimation it forms fine leaflets.

Since anhydrous cobalt chloride is blue, however, the fact that each cobalt ion lies between six chlorine ions is apparently not in harmony with the colour rule. In view of this exceptional behaviour, Professor W. L. Bragg, F.R.S., kindly consented to an *X*-ray examination in his laboratories of anhydrous cobalt chloride itself.

The salt was prepared by dehydrating Kahlbaum's pure hexahydrate (free from iron and nickel) in a current of dry hydrogen chloride. The caked mass was re-ground and re-heated in the stream of gas. This was repeated to obtain a fine powder, which was then filled whilst still hot into thin-walled Lindemann or Röntgen glass tubes, which were quickly sealed off.

The *X*-ray examination (Grime and Santos, *Z. Krist.*, 1934, **88**, 136) confirmed that at atmospheric temperature the crystal structure is of the layer type. The layer order is: Cl, Co, Cl; Cl, Co, Cl, etc.; and each cobalt ion lies between six chlorine ions.

Now it is known that on cooling in liquid air, anhydrous cobalt chloride turns red. The crystal structure was therefore also examined at the temperature of liquid air and was found to be indistinguishable from that at atmospheric temperature. Under these conditions, therefore, the salt conforms to the simple colour rule.

The change in colour without apparent change in the crystal structure demanded further investigation, and it was therefore deemed of interest to examine the (optical) absorption spectrum of solid anhydrous cobalt chloride. It will be shown in the sequel that the absorption spectrum is compounded of that typical of the cobalt atom in association with four chlorine atoms (colour: blue) and of that typical of its association with six groups (colour: red). The compound is essentially red and the change from red to blue with increasing temperature is discussed.

EXPERIMENTAL.

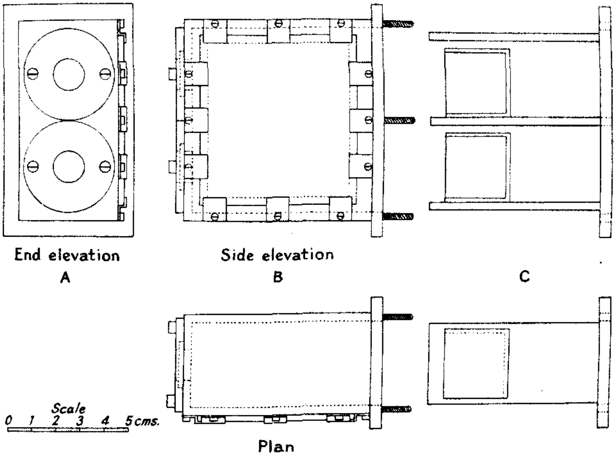
All measurements were made with the Hilger–Nutting spectrophotometer used in the previous investigations. Since all the experiments had to be made with scattered light, the standard lamp-housing and the tube supports provided on the instrument were removed.

Anhydrous cobalt chloride is extremely deliquescent; arrangements therefore had to be made for keeping the specimen under examination in a perfectly dry atmosphere. A cell (Fig. 1) made of brass and blackened all over was provided with a square window at one side (B) to receive the incident light. One end (A) was provided with two circular windows exactly similar to those of the photometer box of the instrument, and the cell was fixed so that the two pairs corresponded exactly. The other end of the cell was closed by a plate (C) fastened by bolts to the flanged end with an air-tight washer between. This plate carried at right angles three metal strips running the length of the cell, and between these were fixed two cube-shaped cardboard boxes; of each of these, one side (facing the square window) was missing for reception of the

incident light, and another (facing the circular windows) for exit of the scattered light at right angles. The other four faces were covered on the inside with the material used as substratum for the blank and with the same coated with anhydrous cobalt chloride for the other beam. Small glass vessels filled with phosphoric oxide were also carried on the strips to maintain a dry atmosphere, and a thermometer was fixed through the end-plate to give the temperature during an observation. The absorption spectrum of a specimen kept in the cell for three days was unchanged over this period.

When filter-paper (or similar material) was used as substratum, a rectangular sheet (4 in. × 2·5 in.) was evenly impregnated with a suitable volume (1·5 c.c.) of aqueous cobalt chloride solution of known concentration. By using solutions of different concentrations, different known

FIG. 1.



amounts of cobalt chloride were taken for examination (see the next paper). The sheet was then carefully air-dried over a flame. With the aid of a templet, a piece of the right shape for covering the inside of the cardboard box was cut out. In this way a constant area was also ensured for the comparison of the relative intensities of absorption with different amounts of cobalt chloride. After the coated paper and the blank had been fixed in the boxes, these were placed between the strips attached to the back of the cell, and the whole was heated in an air oven at 120—125° for ½ hour to ensure complete dehydration. Whilst still hot, the whole fitting was assembled with the remaining part of the cell.

The method used with other materials as substratum, *e.g.*, sintered Jena glass, was similar except that four squares of the material were cut and assembled in metal frames. Impregnation with cobalt chloride solution was done *in situ*.

The source of illumination was a 500 c. p. lamp, housed in an asbestos box with a square tube leading to the window of the cell. Considerable heating occurred, and measurement of the absorption spectrum was delayed until equilibrium was established, when the temperature remained constant at 60° ± 1°.

For the experiments at higher temperatures, the metal cell was replaced by a cylindrical tube of clear silica glass, which was wound with nichrome wire and heavily lagged by means of an asbestos case filled with kieselguhr. An opening was left in the winding and lagging corresponding to the square window of the metal cell. One end of the tube was closed with a plane plate

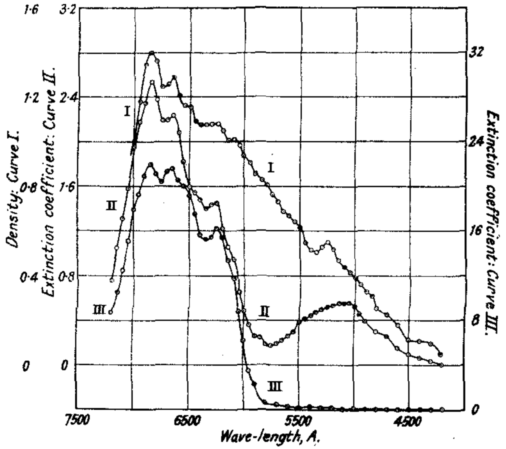
(also of clear silica glass and sealed on) which was covered with asbestos sheet having two small circular holes corresponding to those on the photometer box. The other end of the tube was flanged; this was fitted with a metal end-plate which was bolted to a metal ring bearing against the other side of the flange. The end-plate carried a metal frame bearing the coated box and blank as with the metal cell.

The resistance wire was heated with current from the mains, and a bank of lamps as external resistance enabled any temperature up to 400° to be maintained to within about 2° for the duration of a measurement of the absorption spectrum.

Discussion.

Solid Anhydrous Cobalt Chloride on Cellulose.—The absorption spectrum of solid anhydrous cobalt chloride deposited on filter-paper, by impregnating the paper with aqueous cobalt chloride solution and then dehydrating it in the manner already described, is shown in Fig. 2. The form of the curve is independent of the amount of solid deposited; the intensities of all the bands, however, increase correspondingly with increasing deposition of cobalt chloride in the manner discussed in the following paper. There are also reproduced for comparison the absorption spectrum of the solution of cobalt chloride in moderately concentrated (6·75*N*) aqueous hydrochloric acid, which is partly blue, and of that in very concentrated (13·1*N*) aqueous hydrochloric acid, which is wholly blue.

Fig. 2.



Curve I. Solid anhydrous cobalt chloride.
Curve II. Cobalt chloride in 6·75N-*aqueous* HCl *solution.*
Curve III. Cobalt chloride in 13·1N-*aqueous* HCl *solution.*

It is seen that the initial portion of the absorption spectrum of solid anhydrous cobalt chloride is precisely similar to that of cobalt chloride in aqueous hydrochloric acid solution; the same bands are clearly defined in both: the two principal bands at 6850 A. and 6650 A., the two subsidiary bands at 6250 A. and 6100 A., and also the less pronounced band at 6500 A. These bands which are so much more intense than the others account for the blue colour of anhydrous cobalt chloride. It has been shown that, with cobalt chloride in

aqueous hydrochloric acid solution, these bands are due to the complex $[CoCl_4]''$, and therefore there must be in the solid anhydrous salt also an association between the cobalt ion and four chlorine ions. This is discussed below.

The absorption of cobalt chloride in very concentrated aqueous hydrochloric acid solution falls to practically zero at 5800 A. and remains negligible up to the limit of the visible spectrum. That of solid anhydrous cobalt chloride, however, continues to be appreciable and exhibits a well-defined band at 5250 A.

In this respect solid anhydrous cobalt chloride differs from all the blue cobalt pigments which have been examined (Hill and Howell, *loc. cit.*). The absorption of all the pigments falls rapidly with decreasing wave-length from about 5400 A.; none shows an absorption band at 5250 A. On the other hand, all the red pigments and solutions have a well-defined band between 5300 A. and 5100 A. That this band must be attributed to the red form of anhydrous cobalt chloride is further demonstrated by the fact (see below) that with increasing temperature its intensity decreases whilst that of the bands of the blue form increases, exactly as for the solutions already examined which are partly blue and partly red at a given temperature. Moreover, it is seen that there is a considerable difference in intensity between the two principal bands (6850 A. and 6650 A.) with solid cobalt chloride as with partly blue and partly red solutions (compare the curve for 6·75*N*-hydrochloric acid), whereas with wholly blue solutions the difference is very small (compare the curve for 13·1*N*-acid).

The band of the red form is not due to partial hydration of the salt, since the measurements were made with every precaution against this possibility; moreover, the same band is found (see below) at temperatures above that at which the salt is definitely wholly anhydrous. It is therefore evident that solid anhydrous cobalt chloride is simultaneously blue and red, indicating an association of the cobalt ion with both four and six chlorine ions.

Comparison of the absorption spectrum of solid anhydrous cobalt chloride with that of cobalt chloride in 6·75*N*-aqueous hydrochloric acid solution (Fig. 2) shows that the curves are remarkably similar. If the difference in the absorption at each wave-length be plotted, it is found that the only essential difference between the two curves is that the band at 5850 A. is much more pronounced for the former than for the latter. Marked absorption in this part of the spectrum is characteristic of all the cobalt pigments (see Hill and Howell, *loc. cit.*; see also the curves for solid cobalt chloride in Fig. 3) but is lacking in the blue solutions.

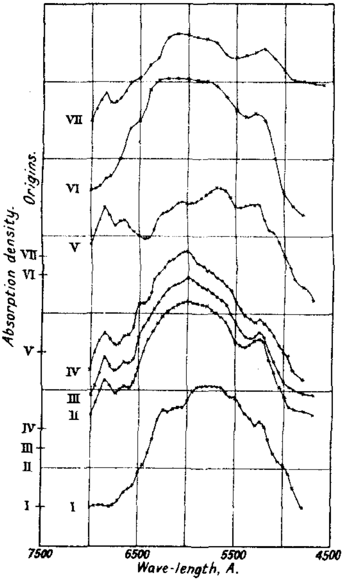
It has been shown that, with cobalt chloride in 6·75*N*-aqueous hydrochloric acid solution, the amount of the blue form is quite small; the extinction coefficient for the first principal band (6850 A.) is only 2·54 as against 22·0 in the wholly blue solution, so the fraction of the cobalt present as the blue form is only 0·115. It is unfortunately not possible to make a similar direct comparison for solid cobalt chloride, because this cannot be converted to the wholly blue form. Some estimate can be made, however, by comparing the intensity of the band of the red form with that of the chief principal band of the blue form in the two instances; the values are, respectively, 0·56 and 2·54 for the solution and 0·55 and 1·4 for the solid. How far the intensity of the band of the red form of solid cobalt chloride is affected by the enhanced absorption of the band at 5850 A. is unknown. The effect is probably small, since with all the blue cobalt pigments, which do not give a band at 5250 A., the absorption falls rapidly from 5400 A. The amount of the blue form present in solid anhydrous cobalt chloride at the working temperature (60°) is therefore probably considerably smaller than in the aqueous solution of cobalt chloride in 6·75*N*-hydrochloric acid at 20°, *i.e.*, less than one-tenth of the whole.

Anhydrous cobalt chloride, however, appears blue to the eye because the intensity of absorption of cobalt in the blue form is far greater than that in the red; thus it has already been shown that the intensity of absorption of $[CoCl_4]''$ is 92·5 times that of $[Co(H_2O)_6]^{\cdot\cdot}$. At the temperature of liquid air, the anhydrous salt is red to the eye and therefore wholly or almost wholly of the red form; since the cobalt ion is in association with six chlorine ions, the colour rule is thus satisfied.

Solid Anhydrous Cobalt Chloride on Other Supports and at Higher Temperatures.—Various materials were tried as supports for the solid cobalt chloride in order to find one suitable for examination of the spectrum at higher temperatures. The curves obtained with some of

these are given in Fig. 3. It is seen that the general form of the curve varies very greatly with the different supports; the absorption spectrum of the deposited solid is profoundly affected by the nature of the substratum. This effect merits further investigation. The same bands are, however, still present but some are much more highly developed on some surfaces than on others. It is important that the band at 5250 A. due to the red form is present in every instance.

FIG. 3.



Solid anhydrous cobalt chloride on :

I. *Porous tile.*
II. *Sintered Jena glass,* 70°.
III. ,, ,, ,, 145°.
IV. ,, ,, ,, 220°.
V. *Ground glass. Deposited from alcoholic solution.*
VI. *Copper gauze. Magnesium oxide as blank.*
VII. *Lead sheet.* ,, ,, ,, ,,
Each ordinate division is 0·4. *The origin of each curve is shown.*

The most suitable surface was sintered Jena glass. This was coated with anhydrous cobalt chloride and the absorption spectrum of the same specimen was measured at a series of temperatures in the manner already described. There was no attack of the glass by the salt over the range examined; after the measurements were complete, the whole of the deposit dissolved in water, leaving the glass as colourless as at first.

Curves of the absorption spectrum at three different temperatures are given in Fig. 3. It is seen that with increasing temperature the intensity of the bands of the blue form increases whilst that of the red form decreases. The effect is not large but is quite definite; taken in conjunction with the fact that cobalt chloride is red at the temperature of liquid air, it establishes that with *increasing temperature* there is a gradual transition from red to blue as for cobalt chloride in moderately concentrated aqueous hydrochloric acid or magnesium chloride solution.

The crystal structure of solid anhydrous cobalt chloride shows that the cobalt ion is centrally situated between six chlorine ions. The gradual change from red to blue with increasing temperature should be explained, according to the colour rule, by increasing association of the cobalt ion with four of the chlorine ions and corresponding decrease of its association with all six. There is, however, no indication that four of the six chlorine ions are differently disposed from the other two; nor was any difference in structure observed at atmospheric temperature from that at the temperature of liquid air. A very small change in the relative positions of the chlorine ions, however, would account for the observed change in colour, and more detailed investigation of the crystal layer might yield interesting information on this point.

SUMMARY.

1. The absorption spectrum of solid anhydrous cobalt chloride deposited on filter-paper is very similar to that of cobalt chloride in aqueous hydrochloric acid or magnesium chloride solution.

2. The bands typical of the cobalt ion in association with four chlorine ions (colour: blue) and the band typical of its association with six groups (colour: red) are all present.

3. At the temperature of liquid air anhydrous cobalt chloride is red to the eye and therefore consists almost wholly of the red form.

4. At the ordinary temperature it is evident from a comparison of the intensity of the absorption bands of the solid with those of solutions of cobalt chloride in aqueous hydrochloric acid, that anhydrous cobalt chloride is still chiefly red. It appears blue to the eye because the intensity of a given amount of cobalt in the blue form is far greater than that in the red.

5. At higher temperatures the intensity of the bands of the blue form increases whilst that of the red form decreases, but even at 350° the red form still persists.

6. The essentially red character of anhydrous cobalt chloride is in accord with the colour rule, since its crystal structure shows that each cobalt ion is surrounded by six chlorine ions.

7. The gradual conversion from red to blue of solid anhydrous cobalt chloride with increasing temperature is exactly comparable with that of the salt in aqueous hydrochloric acid or magnesium chloride solution and should therefore be due to the same cause, *viz.*, increasing association of the cobalt ion with four of the chlorine ions.

8. The crystal structure (determined by the powder method) gives no indication of such change or of any difference in disposition of four of the six chlorine ions, but further investigation of the lattice layer would be of interest.

9. The absorption spectrum of solid anhydrous cobalt chloride deposited on various supports shows that the deposit is affected by the nature of the substratum. Different bands are enhanced by different surfaces.

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203. *The Available Surface of Cellulose.*

By O. RHYS HOWELL and ALBERT JACKSON.

IN the preceding communication an account is given of the absorption spectrum of solid anhydrous cobalt chloride deposited on various supports, including filter-paper. It was deemed of interest to measure the absorption spectrum with different amounts of the deposited solid, since this might afford a novel method of determining the available or real surface of cellulose fibre.

The paper used was made in the Department of Textile Chemistry of this College from a batch of good cotton cellulose originally intended for nitration. The material received only moderate beating, and no addition was made to the "furnish." The paper is therefore composed purely of cotton cellulose. It is an absorbent paper similar to that commonly employed for filtration and is therefore referred to throughout as filter-paper.

Pieces of the filter-paper, all of the same area (10 sq. in.), were impregnated with the same volume (1·5 c.c.) of aqueous solutions of cobalt chloride of different concentrations.

TABLE I.

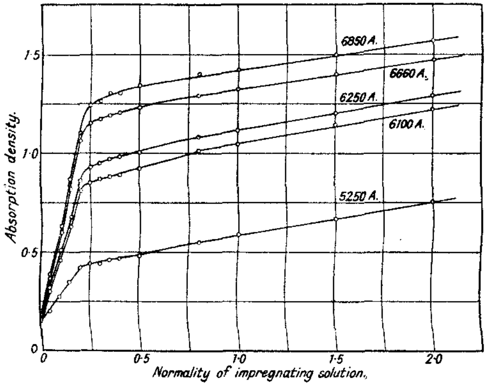
	Extinction coefficient at (A.).				
$CoCl_2$, *N*.	6850.	6660.	6250.	6100.	5250.
0·05	0·39	0·37	0·32	0·30	0·20
0·10	0·63	0·60	0·51	0·46	0·27
0·15	0·87	0·82	0·68	0·63	0·35
0·20	1·10	1·06	0·86	0·81	0·42
0·25	1·24	1·15	0·93	0·85	0·44
0·30	1·26	1·17	0·95	0·87	0·44
0·35	1·30	1·19	0·97	0·88	0·46
0·40	1·30	1·20	0·98	0·89	0·47
0·50	1·34	1·23	1·00	0·92	0·48
0·80	1·40	1·29	1·08	1·01	0·55
1·00	1·42	1·32	1·11	1·04	0·59
1·50	1·50	1·40	1·20	1·14	0·67
2·00	1·57	1·47	1·29	1·22	0·75

Each piece was dehydrated and introduced into the air-tight moisture-free cell, where its absorption spectrum was measured in the manner already described.

Results.—The absorption spectrum of one of the specimens is reproduced and discussed

in the previous communication. The general form of the curve is precisely similar for every specimen; it is independent of the amount of cobalt chloride present, but the intensity of the whole absorption increases with increasing deposition of the salt.

The scale readings (densities) at the four chief bands of the blue form and at the band of the red form for each concentration of solution used for impregnation have been read from the curves; they are given in Table I and plotted in the figure.



Discussion.—From the figure, it is seen that with increasing amount of cobalt chloride the absorption at first increases very rapidly and then gradually merges into a linear relation over which the increase is quite small. Over the initial portion of the curve the surface of the filter-paper is evidently being progressively covered with a primary film of the solid; over the final portion the continued increase in absorption is evidently due to the increasing thickness of deposit. The point at which the two portions intersect is the same for all the bands, *viz.*, at 0·24*N*-aqueous cobalt chloride solution for impregnation, and this must be very approximately the stage at which the surface first becomes covered.

The number of molecules of cobalt chloride deposited on the filter-paper from the known volume of solution of this critical concentration can be calculated. The area occupied by each chloride molecule in the crystal lattice layer can also be calculated. Hence, on the assumption that when the surface is first covered the film of solid is a unimolecular layer corresponding to a single layer of the crystal lattice, the area on which it stands, *i.e.*, the available surface of the filter-paper, can be determined. The requisite data are in Table II.

TABLE II.

Size of filter-paper used = 10 sq. in.	= 64·52 cm.^{2}
Volume of solution used for impregnation	= 1·50 c.c.
Critical concn. of impregnating solution from curve of extinction coefficient	= 0·24*N*
No. of $CoCl_2$ molecules in this volume = $6·06 \times 10^{23} \times 1·5 \times 10^{-3} \times 0·12$	= $10·9 \times 10^{19}$
Area of one $CoCl_2$ molecule in the crystal lattice layer	= 10·9 A.^{2}
Real area of the filter-paper, assuming single lattice layer of $CoCl_2$ = $10·9 \times 10^{19} \times 10·9 \times 10^{-16}$	= $1·19 \times 10^5$ cm.^{2}
Weight of the filter-paper (10 sq. in.)	= 0·877 g.
Available surface per g. = $1·19 \times 10^5/0·877$	= $1·36 \times 10^5$ cm.^{2}
Apparent surface of fibres per g.	= $1·6 \times 10^3$ cm.^{2}
Ratio (Available surface)/(Apparent surface)	= 85

The value for the available surface thus obtained, $1·36 \times 10^5$ cm.^{2}/g., is a maximum value; if the initial coating is multimolecular, the value must be divided by the number of lattice layers constituting the deposit.

The filter-paper used in this investigation has been examined microscopically by Mr. F. W. Bailey, M.Sc.Tech., whom we desire to thank. Two hundred separate pieces of fibre were measured; splitting of the fibres had occurred to a limited extent during beating, and the total apparent surface (including that of the canals) was calculated by using the value 0·621 for the specific volume of cotton cellulose in water (Davidson, *J. Textile Inst.*, 1927, **18**, T175). The value thus found is $1{\cdot}6 \times 10^3$ cm.^{2}/g. (compare Bell, "The Effects of Beating on Fibrous Cellulose," Thesis, Edinburgh University; Strachan, *Proc. Tech. Sect. Paper Makers' Assoc.*, 1926, **6**, 139; Herzog, *Papier-Fabr.*, 1925, **23**, 121; *Naturwiss.*, 1924, **12**, 955). The available surface is therefore about 85 times as great as the apparent surface.

The available surface of wood cellulose has been measured from the absorption compression of water (Stamm, *J. Physical Chem.*, 1929, **33**, 398); the value found is $3{\cdot}1 \times 10^5$ cm.^{2}/g., which is 170 times as great as the apparent surface calculated from microscopical observation (see also Mark, "Physik und Chemie der Cellulose," Berlin, 1932, pp. 163 and 182, for ramie fibre).

These figures are of the same order as those now obtained for cotton cellulose, and afford strong evidence for the truth of the assumption on which they are based, *viz.*, that the initial coating of the solid cobalt chloride consists of a single layer of the crystal lattice.

The original layer may not be wholly continuous. It is seen from the curves that there is a transitional portion before the linear relation begins, and it is possible that over this range the spaces between the almost continuous unimolecular layer are being closed by overlapping of the layers subsequently deposited. The linear relation begins at a concentration about three times as great as that necessary for the production of the original layer, so that (on this assumption) three lattice layers suffice to secure a wholly continuous deposit. Alternatively, it may be argued that the effect of the layers immediately next after the original unimolecular layer is greater than that of those subsequently deposited, and that, after the deposit is about three layers thick, each additional layer produces an approximately equal effect.

It is difficult to compare the change of absorption with concentration for cobalt chloride and that for dyes on textiles (see, *e.g.*, for wool, Cunliffe and Lambert, *J. Soc. Dyers Col.*, 1929, **45**, 313; for cotton, Guelke and Fitzsimons, *Trans. Faraday Soc.*, 1934, **30**, 512). The concentration of vat dyes used (*e.g.*, Blue RC, Blue 3G, Blue GCD, Ciba Blue 2B) reached a value of 2—3%. The number of molecules per g. of cotton present over the range examined is considerably less than for cobalt chloride; for instance, 1% of Ciba Blue gives $1{\cdot}0 \times 10^{19}$ molecules/g. as against $1{\cdot}25 \times 10^{20}$ molecules/g. of cobalt chloride for the original unimolecular layer. Little is known, however, regarding the orientation of dyes on fibres. The molecules of the vat dyes are very large; if we consider only the benzene nuclei, each with an area of 24 A.^{2}, those mentioned above have areas 10 or 20 times that of the cobalt chloride molecule. Therefore, if the molecules are lying flat, the surface they cover is comparable with that of the cobalt chloride in these experiments. If, however, they are oriented wholly or partly vertically, or if they are present in colloidal form, the covering of the surface may not be nearly so complete as that attained with cobalt chloride. Further, the mechanism of the deposition of dyes is not likely to be as simple as that of cobalt chloride, since these substances do not possess the simple layer lattice and have a specific affinity for the fibre.

It is hoped, however, that similar measurements to those now reported will shortly be made with dyes, and that these may yield some information on the molecular occupation of the surface.

A new theory of the structure of cellulose has recently been advanced (Farr and Eckerson, *Contr. Boyce Thompson Inst.*, 1934, **6**, 189, 309; Farr and Sisson, *ibid.*, p. 315; Farr, *Paper Trade J.*, 1935, **101**, T.A.P.P.I.Sect., 183; Farr and Eckerson, *Textile World*, 1936, **86**, 74; Farr, *J. Appl. Physics*, 1937, **8**, 228). It has been demonstrated that in the young cotton fibre there are discrete particles or granules of cellulose, and that as the fibre develops, these arrange themselves into a series of long chains. The particles are covered with and cemented together by a pectic material, the volume of which is an almost negligible part (only about 1%) of the whole. By dissolving away this cementing medium, the particles

constituting the mature fibre can be separated and examined. It is found that " one of the most impressive properties of a mass of particles is their uniformity in size." The particles are about 1·5 μ long and about 1·1 μ broad; they are roughly ellipsoidal in form.

It is interesting to compare the apparent surface of these particles with the available surface found in this investigation. The requisite data are collected in Table III. The particle is regarded as a true ellipsoid of major axis, $a = 1{\cdot}5\ \mu$, and minor axes, $b = c = 1{\cdot}1\ \mu$; the eccentricity $e = \sqrt{(a^2 - b^2)/a^2} = 0{\cdot}68$. The volume of the pectic binding is neglected.

TABLE III.

Dimensions of particle	$= 1{\cdot}5\mu \times 1{\cdot}1\mu \times 1{\cdot}1\mu$
Volume of particle	$= 4/3 \times \pi\mu^3 \times 1{\cdot}5/2 \times 1{\cdot}1/2 \times 1{\cdot}1/2 = 9{\cdot}5 \times 10^{-13}$ cm.^{3}
No. of particles per c.c.	$= 1/9{\cdot}5 \times 10^{13} = 1{\cdot}05 \times 10^{12}$
No. of particles per g.	$= 1{\cdot}05/1{\cdot}6 \times 10^{12} = 6{\cdot}56 \times 10^{11}$
Surface of particle	$= 2\pi b^2\ (1 + \sin^{-1} e/e\sqrt{1 - e^2}) = 2\pi \times 1{\cdot}1^2 \times 2{\cdot}49\mu^2 = 4{\cdot}72 \times 10^{-9}$ cm.^{2}
Surface per g.	$= 6{\cdot}56 \times 10^{11} \times 4{\cdot}72 \times 10^{-8} = 3{\cdot}10 \times 10^4$ cm.^{2}/g.
Ratio (Available surface)/(Particle surface)	$= 1{\cdot}36 \times 10^5/3{\cdot}10 \times 10^4 = 4{\cdot}4$

It is seen (Table III) that the available surface of cellulose is about 4·4 times as great as the surface of the particles regarded as smooth ellipsoids. The particles are, however, known to be composed of micelles of glucose residues and the available surface may well be several times as great as that of smooth particles of the same dimensions.

It may be noted that if the particles are present in the fibre in the same form as in the free state, even the maximum closeness of packing would require a higher value for the amount of cementing medium than that actually observed. If the packing of the particles results in distortion, the surface would be thereby increased and give a somewhat smaller value for the ratio of the available surface to the smooth particle surface.

SUMMARY.

1. The absorption spectrum of solid anhydrous cobalt chloride deposited in different amounts on filter-paper has been measured.
2. The absorption at the maxima of the five best-defined bands has been plotted against the amount of cobalt chloride deposited.
3. All the curves are of precisely the same form and exhibit discontinuity corresponding to the formation of a primary covering.
4. Reasons are given for assuming that this primary coating is unimolecular, *viz.*, a unit layer of the crystal lattice.
5. On this assumption, the area occupied by the cobalt chloride, *i.e.*, the available surface of the filter-paper, has been calculated.
6. The total apparent surface of the filter-paper (calculated from measurement of the constituent fibres under the microscope) is $1{\cdot}6 \times 10^3$ cm.^{2}/g. The available surface is $1{\cdot}36 \times 10^5$ cm.^{2}/g., which is 85 times as great.
7. The value is a maximum one. If the primary film is multimolecular, the value must be divided by the number of unit crystal lattice layers constituting the deposit.
8. The magnitude of the value in relation to the granular theory of cellulose is discussed.

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204. *The Action of Bases on Nitrophenylhydrazines. Part II.*

By A. KILLEN MACBETH and J. R. PRICE.

MACBETH and PRICE (J., 1934, 1637) showed that the action of bases on 2 : 4-dinitrophenylhydrazine gave rise mainly to dinitrobenzene, *mm'*-dinitroazoxybenzene, and 6-nitro-1-hydroxy-1 : 2 : 3-benztriazole, the proportions of the products depending on the concentration of the base. The data available did not warrant the assumption that the amount

of triazole formed was independent of the cation present, but this is now shown to be true in a series of experiments carried out at 20° and 60°. The results (Table I) confirm the previous observation that a minimum yield of triazole is obtained at a certain concentration of alkali, and that simultaneously maxima are recorded in the yields of dinitrobenzene and dinitroazoxybenzene.

Müller and Weisbrod (*J. pr. Chem.*, 1925, **111**, 307) found that the action of hydrazine on 1-chloro-2 : 4-dinitronaphthalene gave rise to dinitronaphthol, dinitronaphthalene, dinitroazonaphthalene, and a nitronaphthatriazole, but did not isolate any of the corresponding 2 : 4-dinitronaphthylhydrazine. We have confirmed their results except that, in agreement with our work on dinitrophenylhydrazine, the supposed dinitroazonaphthalene appears actually to be 4 : 4'-*dinitro*-2 : 2'-*azoxynaphthalene*. The failure to isolate any dinitronaphthylhydrazine and the marked occurrence of dinitronaphthol seemed to us to be connected with the reactivity of the chlorine atom or other group in the 1-position. This suggestion is confirmed, for examination shows that 1-chloro-2 : 4-dinitronaphthalene is some ten times more susceptible to hydrolysis than the corresponding chlorodinitrobenzene (Table II).

Experimental.

Action of Bases on 2 : 4-*Dinitrophenylhydrazine*. The conditions of experiment and the isolation of the products were as previously described (*loc. cit.*), except that the triazole was separated from inorganic salts by extraction with alcohol. The weights of products obtained from 4 g. of 2 : 4-dinitrophenylhydrazine are recorded below, the figures under the heading "Mols." being obtained from these by calculating the number of mols. of product (to the nearest half mol.) per 100 mols. of dinitrophenylhydrazine.

Table I.

Reagent.		Triazole. Wt.	Triazole. Mols.	Dinitrobenzene. Wt.	Dinitrobenzene. Mols.	Dinitroazoxybenzene. Wt.	Dinitroazoxybenzene. Mols.
NaOH	0·24*N* at 20°	0·72	20	0·81	24	1·34	46
,,	0·48*N* ,,	0·45	12·5	0·81	24	1·47	50
,,	0·95*N* ,,	0·38	10·5	0·87	25·5	1·54	53
,,	1·9 *N* ,,	0·36	10	0·85	25	1·54	53
,,	2·6 *N* ,,	0·46	12·5	0·77	22·5	1·49	51
,,	3·6 *N* ,,	0·65	18	0·67	19·5	1·35	46
,,	4·8 *N* ,,	0·88	24	0·64	19	1·16	40
,,	5·7 *N* ,,	1·20	33	0·49	14·5	1·02	35
,,	0·24*N* at 60°	1·0	27·5	0·78	23	1·14	39
,,	0·12*N* ,,	1·5	41	0·70	20·5	0·84	29
,,	0·06*N* ,,	2·34	64·5	0·42	12·5	0·38	26
,,	0·03*N* ,,	2·78	76·5	0·30	9	0·02	0·5
KOH	0·24*N* at 20°	0·69	19	0·85	25	1·38	47·5
,,	0·48*N* ,,	0·49	13·5	0·87	25·5	1·52	52·5
,,	0·95*N* ,,	0·38	10·5	0·85	25	1·56	53·5
,,	1·9 *N* ,,	0·33	9	0·81	24	1·60	55
,,	2·6 *N* ,,	0·45	12·5	0·73	21·5	1·52	52·5
,,	3·6 *N* ,,	0·62	17·5	0·62	18·5	1·41	48·5
,,	4·8 *N* ,,	0·88	24	0·49	14·5	1·22	42
,,	5·8 *N* ,,	1·21	33·5	0·34	10	1·09	37·5
,,	0·24*N* at 60°	0·94	25·5	0·76	22·5	1·18	40·5
,,	0·12*N* ,,	1·46	40	0·68	20	0·86	29·5
,,	0·06*N* ,,	2·36	65	0·44	13	0·40	13·5
,,	0·03*N* ,,	2·76	76	0·24	14	0·04	1·5
Baryta	0·38*N* at 60°	0·76	20·5	0·78	23	1·30	44·5
,,	0·19*N* ,,	1·02	28	0·74	22	1·10	38
,,	0·09*N* ,,	1·74	48	0·62	18·5	0·74	25·5
,,	0·05*N* ,,	2·40	66	0·40	12	0·34	11·5

Reactivity of Halogens.—To an alcoholic solution of the chloro-compound (100 ml. of 0·01*M*-solution) brought to 25° in a thermostat, alcoholic potash (2 ml., *N*) was added and mixed by shaking. After a definite time interval the mixture was poured into hydrochloric acid (5 ml., 0·2*N*), rinsed, and titrated with 0·2*N*-hydrochloric acid. In the case of chlorodinitronaphthalene the salt of dinitronaphthol produced by hydrolysis served as the indicator, the colour changing sharply from deep red to yellow at the end-point. In the case of chlorodinitrobenzene, chloroform was added during the titration; on shaking, it dissolved the free dinitro-

phenol. A satisfactorily sharp end-point was thus reached when the aqueous layer became colourless.

TABLE II.

1-Chloro-2 : 4-dinitrobenzene.				1-Chloro-2 : 4-dinitronaphthalene.			
Time (mins.).	Ml. 0·2*N*-HCl reqd. for titration.	$\log_{10}\frac{b(a-x)}{a(b-x)}$.	*k*.	Time (mins.).	Ml. 0·2*N*-HCl reqd. for titration.	$\log_{10}\frac{b(a-x)}{a(b-x)}$.	$k \times 10^{-1}$.
1	9·4	0·0287	(6·74)	1	7·25	0·2071	(4·87)
2	9·1	0·0453	(5·32)	2	6·3	0·3844	(4·52)
4	8·6	0·0771	4·53	3·5	5·8	0·5594	3·75
5	8·25	0·1036	4·87	4	5·7	0·6097	3·58
8	7·7	0·1541	4·53	5	5·6	0·6690	3·14
10	7·35	0·1942	4·56	6	5·4	0·8293	3·25
15	6·8	0·2762	4·32	6·5	5·4	0·8293	3·0
20	6·45	0·3472	4·08	7	5·3	0·9461	3·17
25	6·1	0·4429	4·16	8	5·25	1·0212	3·0
30	5·8	0·5594	4·38	10	5·1	1·4065	3·3
40	5·5	0·7404	4·35				
Mean *k* (excluding values in parentheses)			4·42				$3·27 \times 10^{-1}$
Mean *k* (from slope of the curve)			4·36				$3·25 \times 10^{-1}$

a = Initial concentration of potassium hydroxide; b = initial concentration of the chloro-compound; x = change in concentration of the reactants.

Action of Hydrazine Hydrate on 1-*Chloro*-2 : 4-*dinitronaphthalene*.—Following the method of Müller and Weisbrod (*loc. cit.*) chlorodinitronaphthalene (25 g.) was refluxed in alcohol (180 ml.) with excess of hydrazine hydrate (20 ml. of 50%) for 6 hours. After separation from dinitronaphthalene, dinitronaphthol, and 5-nitro-3-hydroxy-αβ-naphtha-1 : 2 : 3-triazole (det. pt. 235°), the residue was dissolved in aqueous sodium hydroxide, and on acidification a reddish-brown solid was precipitated. This on crystallisation from nitrobenzene gave dark red, microscopic, twinned crystals of 4 : 4′-*dinitro*-2 : 2′-*azoxynaphthalene*, m. p. 305—306°, which were no longer soluble in alkali (Found: C, 61·4, 61·6; H, 3·2, 3·5. $C_{20}H_{12}O_5N_4$ requires C, 61·85; H, 3·1%).

JOHNSON CHEMICAL LABORATORIES, UNIVERSITY OF ADELAIDE. [*Received April 28th*, 1937.]

205. *The Mercuration of Nitrotoluidines.*

By ARCHIBALD E. GODDARD.

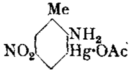
ALTHOUGH the mecuration of nitroaniline has been carried out (Kharasch, Lommen, and Jacobson, *J. Amer. Chem. Soc.*, 1922, **44**, 793), no work has been done on substituted nitroanilines. The following investigation was undertaken to see whether the substitution of the methyl group in the nucleus affected the formation of diacetoxymercuri-compounds and of quinoneimides.

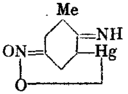
4-Nitro-*o*-toluidine on mercuration in alcoholic solution yields *5-acetoxymercuri-4-nitro-o-toluidine*. The orientation is established by replacing the acetoxymercuri-group by bromine or iodine. When heated alone, with sodium hydroxide, or boiled with alcohol or water for a prolonged period, the compound is transformed into a quinoneimide.

The foregoing changes apply to all the following compounds. It was found impossible to introduce mercury into position 3 or 6 as well as into 5.

In 5-nitro-*o*-toluidine the amino- and the nitro-group are in the para-position, which corresponds to *p*-nitroaniline. The latter yields a mono- and a di-substituted mercury

(I.)





(II.)

compound, together with a quinoneimide, but 5-nitro-*o*-toluidine gives no diacetoxymercuri-compound, and the mercury enters the ring in position 3. The compound and its quinoneimide may be represented by (I) and (II) respectively. The product (II) may be again changed into (I) by treating it with glacial acetic acid.

6-Nitro-*m*-toluidine, which again has the amino- and the nitro-group in the para-position, behaves presumably in the same way as the 5-nitro-*o*-toluidine, the mercury entering the ring in position 4, *i.e.*, ortho to the amino-group. Since 5-bromo-6-nitro-*m*-toluidine is not obtained when the mercury derivative is treated with bromine in acetic acid, the mercury must be in position 4, but 4-bromo-6-nitro-*m*-toluidine is not described in the literature, so direct comparison cannot be made. The acetoxymercuri-compound was only obtained associated with a molecule of water, any attempt to remove the latter merely giving the quinoneimide.

The mercury derivative from 2-nitro-*p*-toluidine is mercurated in position 5, as it yields 5-chloro-2-nitro-*p*-toluidine on treatment with chlorine and calcium chloride in alcoholic solution.

Since no monohalogen derivatives of 3-nitro-*p*-toluidine are known, it is not possible to state definitely whether the mercury has entered position 5 or 6, but judging from the foregoing results it is most probably in position 5.

The chief difficulty encountered in the production of the above compounds has been the elimination of nitrotoluidines from the final products.

Experimental.

The amounts of reacting substances are shown in the following table. The nitrotoluidine was dissolved in the alcohol, the mercuric acetate in the water, and the respective solutions brought to their boiling points before mixing. The whole was then heated for the time shown.

No.	Nitrotoluidine, g.	Alcohol, c.c.	Mercuric acetate, g.	Water, c.c.	Time, mins.
1	1 : 2 : 4, 12·5	150	37	100	180
2	1 : 2 : 5, 25	300	75	200	75
3	1 : 3 : 6, 10	150	30	200	120
4	1 : 4 : 2, 10	150	30	200	270
5	1 : 4 : 3, 20	25	60	200	120

(1) The residue (13 g.) was boiled with a mixture of alcohol (75 c.c.) and glacial acetic acid (15 c.c.). The resulting *quinoneimide*, m. p. about 250°, was brownish maroon (Found: Hg, 57.2. $C_7H_6O_2N_2Hg$ requires Hg, 57·2%).

4-*Nitro-5-acetoxymercuri-*o*-toluidine.* The filtrate from the foregoing preparation was concentrated, and the sticky product solidified by agitation with alcohol. The solid was boiled with alcohol (80 c.c.) and glacial acetic acid (5 c.c.), and filtered off. The filtrate gave an orange precipitate on dilution with water. Repeated crystallisation from alcohol–acetic acid yielded orange crystals, m. p. 212° (Found: Hg, 49·1. $C_9H_{10}O_4N_2Hg$ requires Hg, 49·8%). The quinoneimide on recrystallising from glacial acetic acid gave the same product. Treatment with bromine in acetic acid gave 5-bromo-4-nitro-*o*-toluidine, m. p. 118—119° (Found: Br, 34·5. Calc. for $C_7H_7O_2N_2Br$: Br, 34·6%). 5-Iodo-4-nitro-*o*-toluidine, m. p. 109°, was also obtained, the yield in both cases being quantitative.

(2) 5-*Nitro-3-acetoxymercuri-*o*-toluidine.* The cooled filtrate gave a solid (12 g.) on treatment with water. This was boiled with alcohol (100 c.c.) containing acetic acid (3 c.c.); orange plates separated on cooling, m. p. 223° after sintering at 190° (Found: Hg, 49·0. $C_9H_{10}O_4N_2$ requires Hg, 48·8%).

The foregoing product (7 g.) was boiled with dilute sodium hydroxide solution, maroon metallic needles of the *quinoneimide* resulting, which darkened but did not melt at 300° (Found: Hg, 57·2. $C_7H_6O_2N_2Hg$ requires Hg, 57·2%). Replacement of the mercury by bromine gave 3-bromo-5-nitro-*o*-toluidine, m. p. 180·3—181·3°.

(3) 6-*Nitro-4(?)-acetoxymercuri-*m*-toluidine* (13·2 g.) separated from the filtrate and was boiled with 200 c.c. of alcohol. The terra-cotta residue (9 g.) was dissolved in hot acetic acid, treated with water and slowly evaporated. Brownish-yellow needles separated, sintering at 280°, but unmelted at 300° (Found: Hg, 46·8. $C_9H_{12}O_5N_2Hg$ requires Hg, 46·8%).

The preceding compound (0·5 g.), when heated with 10*N*-sodium hydroxide, gave a crystalline maroon product (Found: Hg, 57·3. $C_7H_6O_2N_2Hg$ requires Hg, 57·2%).

(4) 2-*Nitro-5-acetoxymercuri-*p*-toluidine.* The clear solution gave an orange precipitate on standing; repeated crystallisation from a solution containing water (50 c.c.), alcohol (30 c.c.), and acetic acid (5 c.c.) yielded a high-melting solid (7·1 g.) (Found: Hg, 48·9. $C_9H_{10}O_4N_2Hg$ requires Hg, 48·8%).

The *quinoneimide* was a crystalline maroon compound, isolated by the aid of 10*N*-sodium

hydroxide (Found: Hg, 57·3. $C_7H_8O_2N_2Hg$ requires Hg, 57·2%). Chlorine in alcoholic calcium chloride converted it into 5-chloro-2-nitro-*p*-toluidine, m. p. 130°.

(5) 3-*Nitro*-5(?)-*acetoxymercuri*-p-*toluidine* was obtained when the quinoneimide was recrystallised from a little acetic acid, orange-yellow crystals separating (Found: Hg, 48·7. $C_9H_{10}O_4N_2Hg$ requires Hg, 48·8%).

The residue (10 g.) from the reaction mixture was boiled with water (250 c.c.) containing a few drops of acetic acid, and after filtration the hot liquid was treated with a little sodium hydroxide solution. The dark chocolate, crystalline precipitate was unmelted at 300° (Found: Hg, 56·9. $C_7H_6O_2N_2Hg$ requires Hg, 57·2%).

The author thanks the Government Grants Committee of the Royal Society for a grant.

"THALLIA," GLENFIELD FRITH DRIVE, GROBY RD., LEICESTER. [*Received, March 17th, 1934.*]

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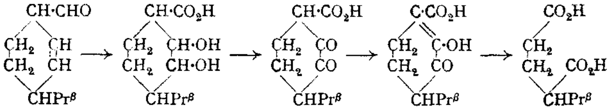
206. *The Carbonyl Constituents of Eucalyptus Oils. Part I. The Occurrence of Cryptal.*

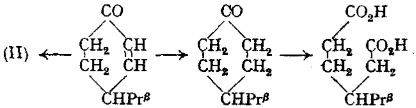
By P. A. BERRY, A. KILLEN MACBETH, and T. B. SWANSON.

AN examination by Penfold (J., 1922, **121**, 266) showed that the "aromadendral" previously isolated from various eucalyptus oils by Smith (*J. Roy. Soc. New South Wales*, 1900, **34**, 286; *Pharm. J.*, 1905, **75**, 356, 382; *Trans. Roy. Soc. South Australia*, 1916, **40**, 485) was in fact a mixture of cuminal and phellandral, and occurring with it was the substance cryptal which had already been isolated on several occasions by Smith and his co-workers (Baker and Smith, "A Research on the Eucalypts and Their Essential Oils," 2nd edn., Sydney, 1920, pp. 61, 386, 387). Cryptal was regarded as an aldehyde isomeric with phellandral, and later Penfold and Simonsen (J., 1930, 403) considered it to be *l*-4-*iso*propyl-Δ^2-*cyclo*hexenal (I), since, when oxidised in acetone solution by potassium permanganate, it yielded *d*-α-*iso*propylglutaric acid (II) in practically quantitative yield.



(I.) (II.)

The constitution as a ten-carbon aldehyde was not in accord with analytical results we had obtained on examining some derivatives of the so-called cryptal from *E. cneorifolia*, but Cahn, Penfold, and Simonsen (J., 1931, 1366) showed that a sample of "cryptal" from this source, although agreeing excellently in physical properties with the sample of cryptal used in the previous work, was in fact the 9-carbon ketone *l*-4-*iso*propyl-Δ^2-*cyclo*hexen-1-one (III), since oxidation of the corresponding reduced ketone gave β-*iso*propyladipic acid (IV).



(III.) (IV.)

Our results entirely confirm this constitution, for the same oxidation product has been isolated from the reduced ketone, whereas the ketone itself yields α-*iso*propylglutaric acid. Further, the αβ-unsaturation is confirmed by the isolation of a characteristic hydrosulphide (Hooper, Macbeth, and Price, J., 1934, 1147). The occurrence of cryptal in eucalyptus oils would thus appear to be problematical, but Cahn, Penfold, and Simonsen (*loc. cit.*) were

of opinion that " there would appear to be no doubt of its separate existence and it is possible that it is only present during certain seasons." Apart from the fact that *l*-4-*iso*propyl-Δ^2-*cyclo*hexen-1-one yields the same oxidation product as that on which the structure of cryptal is based, two further significant observations were made in the original paper. In the first place attempts to oxidise cryptal to the corresponding acid were uniformly unsuccessful; and also the *oxime*, when heated with acetic anhydride, was not dehydrated to the nitrile and the reaction was thought to be proceeding abnormally. The absence of an aldehyde group is thus definitely suggested, and we have now examined the oxime derived from *l*-4-*iso*propyl-Δ^2-*cyclo*hexen-1-one. Its physical properties agree closely with those recorded for cryptal oxime, and, further, on treatment with acetic anhydride it yields a crystalline product identical with that obtained by Penfold and Simonsen from the alleged cryptal. This strengthens the view that 4-*iso*propyl-Δ^2-*cyclo*hexenal has not hitherto been isolated from eucalyptus oils. This opinion is further supported by the fact that our examination of the " cryptal " component of a number of oils has invariably shown the presence only of the ketone. This examination has included several samples of *E. polybractea* oil, samples of *E. hemiphloia* from two districts in Victoria, the " cryptal " from the oil of the same species in New South Wales, and numerous distillations of *E. cneorifolia*. A large-scale fractionation of the oil of the last class also failed to give any indication of the occurrence of the aldehyde mixed with the ketone fraction; and we have not succeeded in isolating a dimedon derivative. The results of the seasonal examination of *E. cneorifolia*, which has not disclosed any evidence of such a kind, will be communicated later.

EXPERIMENTAL.

Isolation of l-4-iso*Propyl*-Δ^2-cyclo*hexen*-1-*one*.—Previous methods of separating the carbonyl constituents of eucalyptus oils consisted in treatment with sodium bisulphite solution, the phellandral and cuminal being combined as an insoluble derivative whilst the ketone was dissolved and recovered from the filtrate. A better procedure appears to be that adopted in the present work, in which the oil, or the fraction rich in carbonyl compounds, is shaken with neutral sodium sulphite solution (35% wt./wt. $Na_2SO_3,7H_2O$) to remove the ketone. If the oil is treated with more than five times its volume of neutral sulphite solution and the sodium hydroxide set free is periodically neutralised with sulphuric acid (10%), a satisfactory extraction of the ketone takes place and the process is completed in about an hour. The ketone is recovered from the solution by the addition of sodium hydroxide (40% solution) in the presence of ether. The original oil, after the removal of the ketone, is then shaken for 8—10 hours at laboratory temperature with twice its volume of saturated sodium bisulphite solution to recover the cuminal and phellandral, which are purified in the usual way. If the first extraction of the ketone is not complete, a further yield is obtained by the addition of sodium hydroxide to the bisulphite filtrate after removal of unabsorbed oil by ether.

In all cases the ketone was purified by re-treatment with neutral sulphite solution and fractional distillation. It was obtained as a clear liquid, α_D ranging from $-54{\cdot}5°$ to $-80{\cdot}4°$ in various samples and b. p. from 94°/5 mm., 104°/13 mm., to 110—112°/25 mm. It is thus not stereochemically pure (Galloway, Dewar, and Read, J., 1936, 1595). In its identification the following derivatives were employed: semicarbazone, m. p. 187—188° (Found: C, 61·6; H, 8·9. Calc.: C, 61·5; H, 8·7%); *p*-nitrophenylhydrazone, m. p. 168—169° (Found: C, 65·9; H, 6·75. Calc.: C, 65·9; H, 6·9%); 2 : 4-dinitrophenylhydrazone, m. p. 138° (Hooper, Macbeth, and Price, *loc. cit.*) (Found: C, 56·7; H, 5·6. Calc.: C, 56·6; H, 5·7%); this derivative only gives the high m. p. recorded after some ten crystallisations from ethyl alcohol (compare Galloway, Dewar, and Read, *loc. cit.*, m. p. 129—130°); hydrosulphide, which is readily prepared by passing hydrogen sulphide into a solution of the ketone in absolute alcohol in the presence of anhydrous sodium carbonate; recrystallised from chloroform, m. p. 206—207° (Found: S, 10·2. Calc.: S, 10·3%) (Hooper, Macbeth, and Price, *loc. cit.*).

Oxime of l-4-iso*Propyl*-Δ^2-cyclo*hexen*-1-*one*.—The ketone (35 g.) was refluxed for an hour with alcohol (350 g.) and hydroxylamine hydrochloride (20 g.) in the presence of anhydrous sodium acetate. After removal of the major part of the alcohol the *oxime* was distilled in steam, extracted in ether, dried (anhydrous sodium sulphate), recovered, and distilled under reduced pressure, yielding a thick clear oil (22 g.), b. p. 160—161°/33 mm., $n_D^{20°}$ 1·5160 (Found: C, 70·8; H, 9·9. $C_9H_{15}ON$ requires C, 70·6; H, 9·8%).

A solution of the oxime in acetic anhydride (10 parts) containing anhydrous sodium acetate was refluxed for 2 hours, cooled, and poured into water. The dark brown oil obtained, after being washed in ether with sodium carbonate solution and dried (potassium carbonate), was distilled under reduced pressure. The fraction, b. p. 200—212°/26 mm., was a viscous oil which crystallised and after draining on a porous tile was obtained in long needles, m. p. 103°, from light petroleum (b. p. 60°). This is evidently identical with the product obtained by Cahn, Penfold, and Simonsen (*loc. cit.*) and is being further examined.

Reduction of 1-4-iso*Propyl*-Δ^2-cyclo*hexen*-1-*one*.—The catalytic reduction of the ketone by hydrogen in the presence of palladised charcoal (as described by Cahn, Penfold, and Simonsen, *loc. cit.*) was carried out on several occasions for its further identification in various oils. The amounts of hydrogen absorbed in the various experiments (1125—1173 c.c.) were nearly theoretical (1136 c.c.) for the amount of ketone treated (7 g.). The product, 4-*iso*propyl*cyclo*hexan-1-one, was identified by the semicarbazone, m. p. 188—189°, the *p*-nitrophenylhydrazone, m. p. 123—124°, and also the 2 : 4-dinitrophenylhydrazone, which crystallised at once when the ketone (1 g.) in alcohol (20 c.c.) was added to 2 : 4-dinitrophenylhydrazone (1 g.) in concentrated sulphuric acid (2 c.c.) and alcohol (15 c.c.) and on recrystallisation from alcohol formed orange-yellow plates, m. p. 119—120° (Found : C, 56·4; H, 6·15. Calc. for $C_{15}H_{20}O_4N_4$: C, 56·25; H, 6·25%) (compare Macbeth and Price, J., 1935, 151).

The oxidation of *l*-4-*iso*propyl*cyclo*hexan-1-one as described by Cahn, Penfold, and Simonsen (*loc. cit.*) yielded β-*iso*propyladipic acid, m. p. 83—84° (recrystallised from water).

Large-scale Distillations of E. cneorifolia.—As the main object of the work was a search for cryptal associated with the ketone, distillations of *E. cneorifolia* on a commercial scale were carried out under supervision at Kangaroo Island, South Australia, samples being examined at different stages of the distillation. Typical results are recorded in the table, and it is evident that the aldehydes distil without much variation until the final stage; the percentage is then about doubled. No cryptal was found in any of the fractions.

Time.	Oil in distillate, lb.	$d_{15.5°}^{15.5°}$.	Aldehydes, %.	Cineole, %.	Rotation of oil (l = 1 dm.).
11.15 a.m.	—	—	—	—	—
11.25 ,,	3	0·9215	8·25	75·6	−3·14°
11.30 ,,	1·75	0·9224	9·07	74·2	−2·9
11.35 ,,	3·5	0·9227	8·62	73·5	−2·97
11.45 ,,	3·5	0·9237	9·75	72·8	−3·62
12.5 p.m.	3·5	0·9221	9·53	70·5	−4·14
12.30 ,,	2·25	0·9209	11·1	68·6	−4·27
2.30 ,,	4·5	0·9233	18·0	54·6	−7·74

The cineole content was determined by the B.P. *o*-cresol method, and the aldehydes were estimated by the neutralisation of N/2-alcoholic sodium hydroxide by the oil in the presence of 5% hydroxylamine hydrochloride solution, bromophenol-blue being used as indicator. The results were calculated in terms of $C_{10}H_{14}O$, as subsequent work showed that the aldehydes and ketone were present in approximate amounts in agreement with this formula. Each c.c. of alkali is thus equivalent to 0·075 g. of aldehyde (including the ketone).

Further large-scale work involved the steam distillation of three drums of commercial *E. cneorifolia* oil supplied by a Kangaroo Island distiller from leaf cut during the autumn months. The last fractions distilling from 134 gallons of oil in three separate experiments were combined and gave 6·5 gallons of oil, which was again fractionally steam-distilled. The first fraction (1 gallon) had α_D − 7·32°, $d_{15.5°}^{15.5°}$ 0·9301, cineole 67%; the second fraction (3 gallons) had α_D − 17·6°, $d_{15.5°}^{15.5°}$ 0·9427, cineole 40·8%, aldehydes 36%; and a third fraction (1·5 gallons) had $\alpha_D^{20°}$ − 35·01, $d_{15.5°}^{15.5°}$ 0·9622, cineole 22·6% and aldehydes 40%. After shaking with 5% sodium hydroxide solution and subsequent washing, portions of the fractions were treated by the method already outlined for the separation of the carbonyl compounds. Cuminal (semicarbazone, m. p. 210—211°; 2 : 4-dinitrophenylhydrazone, m. p. 238°) and *l*-phellandral [semicarbazone, m. p. 202—203°; *p*-nitrophenylhydrazone, m. p. 169—170° (Found : C, 66·8; H, 7·4. Calc.: C, 66·9; H, 7·3%); atmospheric oxidation to the corresponding carboxylic acid, m. p. 143·5—144·5°] were isolated. The latter was further characterised by its 2 : 4-dinitrophenylhydrazone, which separated on the addition of the aldehyde (1 g.) in alcohol (20 c.c.) to 2 : 4-dinitrophenylhydrazine (1 g.) in concentrated sulphuric acid (2 c.c.) and alcohol (15 c.c.). *Phellandral* 2 : 4-*dinitrophenylhydrazone* is sparingly soluble in alcohol, but easily soluble in chloroform. It is obtained on recrystallisation from alcohol–chloroform in deep orange needles,

m. p. 202—203° (Found: C, 57·6; H, 5·7. $C_{16}H_{20}O_4N_4$ requires C, 57·8; H, 6·0%). *l*-4-*iso*-Propyl-Δ^2-*cyclo*hexen-1-one also was isolated and identified by its derivatives; but cryptal was not found.

Eucalyptus polybractea. Two 4-gallon samples of the oil of *E. polybractea* from Victoria were examined. The oil from one-year old leaf had $d_{15.5°}^{15.5°}$ 0·9270, cineole 87·1%, alcohols 7·6%, and aldehydes 2·5%. Treatment in the usual way with sodium sulphite, followed by sodium bisulphite, led to the isolation of cuminal, *l*-phellandral, and *l*-4-*iso*propyl-Δ^2-*cyclo*hexen-1-one. The same products were obtained from the oil from two-year old leaf, which had $d_{15.5°}^{15.5°}$ 0·9279, cineole 91·0%, alcohols 2·9%, and aldehydes 2·6%. In neither case was any cryptal detected.

Eucalyptus hemiphloia. Two samples of the oil of this species from different districts in Victoria were examined. The first, from the Rushworth district, was obtained through the courtesy of the Inspector General of Forests, Mr. C. E. Lane Poole. It had α_D − 17·2°, ester value 25·9, alcohols 19·1%, cineole 16·9%, and aldehydes 19·4%. The ketone (37·5 g.) was isolated by the usual treatment and the proportion of ketone in the total aldehydes was some 36%. Cuminal and *l*-phellandral also were isolated; but no cryptal was found. For the second sample, from the Somerton district, we are indebted to Mr. S. G. Reilly of Messrs. J. Bosisto & Co., Richmond, Victoria. It had α_D − 21·8°, cineole 19·2%, and aldehydes 22·6%. In this case also the ketone was isolated and identified, but cryptal was not detected.

Mr. A. R. Penfold kindly supplied a sample of "cryptal" from the oil of *E. hemiphloia* from New South Wales. It also was identified as *l*-4-*iso*propyl-Δ^2-*cyclo*hexen-1-one, giving the characteristic hydrosulphide and other derivatives.

We are indebted to Messrs. A. M. Bickford & Co. Ltd., Adelaide, for the large-scale distillations and to the others specified who helped us to obtain supplies of the various oils.

THE JOHNSON CHEMICAL LABORATORIES,
THE UNIVERSITY OF ADELAIDE. [*Received, May 10th, 1937.*]

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207. *The Characterisation of Basseol, a Tetracyclic Triterpene Alcohol, and its Isomerisation to β-Amyrenol.*

By J. H. BEYNON, I. M. HEILBRON, and F. S. SPRING.

THE non-saponifiable matter of shea nut oil has been shown to contain illipene, β-amyrenol, lupeol, and a monohydric alcohol, m. p. 109·5° (Heilbron, Moffet, and Spring, J., 1934, 1583). With a view to locating a more prolific source of the last compound, for which the name basseol has been proposed (Beynon, Heilbron, and Spring, *Nature*, 1936, **138**, 1017), the non-saponifiable matters both of the cambium of the shea and of the bark of *Alstonia scholaris* have been examined. The fat from the latter does not contain basseol, the main components being the amyrenols, the β-isomer largely predominating, and lupeol (compare Ultée, *Chem. Weekblad*, 1914, **11**, 456).

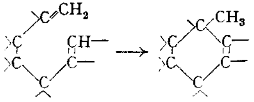
From the shea cambium, lupeol, α-amyrenol and basseol have been isolated, but since the yield of basseol does not compare favourably with that from the nut oil, the material used in the present investigation was obtained by the previously described method. Whereas shea nut oil contains β-amyrenol, only the α-isomer appears to be present in the cambium.

A preliminary examination of basseol (Heilbron, Moffet, and Spring, *loc. cit.*) showed that it is a diethenoid alcohol of the molecular formula $C_{30}H_{50}O$ or $C_{29}H_{48}O$. A decision in favour of the former has now been made, first, by the determination of the equivalent of basseol acetate and, secondly, by the isomerisation of this acetate to β-amyrenyl acetate by a variety of reagents such as bromine, the halogen acids, formic acid, and sulphuric acid. In view of this facile conversion of the diethenoid tetracyclic basseol into the monoethenoid pentacyclic β-amyrenol, a structural study of the former becomes of considerable importance in so far as the molecular configuration of the triterpene series as a whole is concerned.

A spectrographic examination of basseol acetate establishes that the two ethylenic linkages are not conjugated; catalytic hydrogenation shows that it absorbs only one mole

of hydrogen, giving *bassenyl acetate* (dihydrobasseol acetate), m. p. 119—120°, which is completely resistant to further hydrogenation, in this respect resembling β-amyrenyl acetate (Ruzicka, Huyser, Pfeiffer, and Seidel, *Annalen*, 1929, **471**, 21). Bassenyl acetate gives a yellow coloration with tetranitromethane in chloroform solution, absorbs one atom of oxygen on titration with perbenzoic acid, and, in contrast to basseol acetate, does not undergo ring closure.

The reactive ethylenic linkage of basseol has been diagnosed as an exocyclic methylene group, since basseol acetate, in contradistinction to bassenyl acetate, gives formaldehyde (20%) on ozonolysis; consequently the isomerisation of basseol to β-amyrenol may be represented by the scheme :—



From the non-volatile fraction of the products obtained by the ozonolysis of basseol acetate, β-amyrenyl acetate oxide (Spring, J., 1933, 1345) has been isolated; the oxidative degradation of both basseol and its dihydro-derivative is being further investigated.

Experimental.

The Non-saponifiable Matter of Shea Cambium.—The ground cambium (3 kg.) from large-girth trees was heated under reflux with successive portions of alcohol (6, 4, 4, 4 l.) for 3-hour periods. The combined extract was concentrated to approximately one quarter bulk and after the addition of a solution of potassium hydroxide (500 g.) in water (200 c.c.) was heated under reflux for 5 hours. After dilution with water, the solution was extracted with ether, and the extract washed successively with dilute hydrochloric acid and water. Removal of the solvent from the dried extract gave a light brown, resinous solid (50 g.), which showed no tendency to crystallise from a variety of solvents.

α-Amyrenyl Acetate.—The non-saponifiable matter (50 g.) was heated under reflux with acetic anhydride (150 c.c.) and anhydrous sodium acetate (25 g.) for 2½ hours and poured into alcohol (200 c.c.). The solid (A) separating overnight (m. p. 130—170°) was recrystallised from alcohol to give a crop (12 g.), m. p. 185—200°, repeated crystallisation of which from ethyl acetate yielded α-amyrenyl acetate (1·5 g.) in colourless plates, m. p. 222°, unchanged by further crystallisation or by admixture with an authentic specimen from *Manila elemi*; $[\alpha]_D^{20°}$ + 76° (l = 1, c = 5·0 in chloroform) (Found: C, 82·1; H, 11·0. Calc. for $C_{32}H_{52}O_2$: C, 81·95; H, 11·2%).

Basseol Acetate.—After concentration and standing, the filtrate from fraction A deposited a solid (10 g.), m. p. 85—95°, which after two crystallisations from ethyl acetate yielded rosettes of needles (2 g.), m. p. 141°, $[\alpha]_D^{18.5°}$ + 23° (l = 1, c = 1·95 in chloroform), unchanged by further crystallisation or by admixture with the acetate obtained by Heilbron, Moffet, and Spring (*loc. cit.*) from shea nut fat (Found: C, 81·9; H, 11·0. Calc. for $C_{32}H_{52}O_2$: C, 81·95; H, 11·2%).

Lupeol Benzoate and α-Amyrenyl Benzoate.—Concentration of the alcoholic mother-liquors from the fraction, m. p. 185—200°, gave successive crops which could not be further purified by crystallisation. These crops and their mother-liquors were combined, the solvent mixture removed under reduced pressure, the residual solid hydrolysed by heating under reflux with 7% alcoholic potassium hydroxide (500 c.c.) for 6 hours, and the solution largely diluted with water. The crystalline solid (10 g.) isolated by means of ether was benzoylated by heating under reflux for 5 hours with benzoyl chloride (20 c.c.), pyridine (15 c.c.), and dry benzene (100 c.c.). Removal of the solvent under reduced pressure yielded an oil, which was extracted with ether, the extract being washed successively with dilute sodium hydroxide solution, dilute sulphuric acid, and water. The solid obtained after removal of the solvent was repeatedly crystallised from benzene–alcohol; lupeol benzoate was then obtained in plates, $[\alpha]_D^{20°}$ + 60·3° (l = 1, c = 4·0 in chloroform), m. p. 265° either alone or in admixture with an authentic specimen (Found: C, 83·7; H, 10·1. Calc. for $C_{37}H_{54}O_2$: C, 83·7; H, 10·3%). Concentration of the mother-liquor from the first crystallisation of lupeol benzoate gave a solid, m. p. 85—95°, which on repeated crystallisation from benzene–alcohol yielded α-amyrenyl benzoate in hard needles, m. p. 194°, not depressed on admixture with an authentic specimen.

Molecular Weight of Basseol Acetate.—The acetate (400 mg.) was heated under reflux for 2 hours with alcoholic potassium hydroxide solution (40 c.c.; titre, 28·1 c.c. 0·1*N*-hydrochloric acid). The solution was diluted with alcohol (60 c.c.) and titrated with 0·1*N*-hydrochloric acid and phenolphthalein. The titre was standardised by comparison with that of a blank consisting of the same volume of alcoholic potassium hydroxide solution and alcohol. Basseol acetate: Found, *M*, 465, 464; $C_{32}H_{52}O_2$ requires *M*, 468. Cholesteryl acetate: Found, *M*, 431, 432; $C_{29}H_{48}O_2$ requires *M*, 428.

Isomerisation of Basseol Acetate.—(a) *Bromine.* A solution of bromine (0·68 g.; 2 mols.) in dry ether (50 c.c.) was added to basseol acetate (1 g.) in dry ether (100 c.c.), and the mixture set aside at room temperature for 8 hours and at − 5° for 10 hours. The oil obtained after removal of the solvent under reduced pressure was crystallised from ethyl acetate, from which β-amyrenyl acetate (0·5 g.) separated in needles, m. p. 236°, $[\alpha]_D^{19°}$ + 77° (*l* = 1, *c* = 0·05 in chloroform) (Found: C, 81·8; H, 11·4. Calc. for $C_{32}H_{52}O_2$: C, 81·95; H, 11·2%). The identity of the specimen was confirmed by hydrolysis and conversion of the crude amyrenol into the benzoate, which separated from benzene–alcohol in plates, m. p. 230° (Found: C, 83·6; H, 10·6. Calc. for $C_{37}H_{54}O_2$: C, 83·7; H, 10·3%). Furthermore, the melting points of the acetate and benzoate were unchanged on admixture with authentic specimens.

Solutions of basseol acetate (0·3 g.) in (b) a solution of sulphuric acid in acetic acid (2%, 30 c.c.), (c) formic acid (98%, 100 c.c.), (d) ethereal hydrogen bromide (3%, 150 c.c.), and (e) chloroform (75 c.c.) saturated at 0° with dry hydrogen chloride, were kept at 0° for 24 hours. In each case β-amyrenyl acetate (20, 13, 40, and 90% respectively) was isolated.

Bassenyl Acetate.—Basseol acetate (2 g.) in glacial acetic acid (140 c.c.) was shaken with hydrogen in the presence of Adams's catalyst (1 g.) at 75°, the hydrogen absorption (1 mol.) ceasing after 1 hour. The solution was diluted with water (200 c.c.), and the precipitated solid crystallised from aqueous alcohol, from which *bassenyl acetate* (1·8 g.) separated in needles, m. p. 119—120°, $[\alpha]_D^{20°}$ + 32·5° (*l* = 1, *c* = 0·8 in chloroform) (Found: C, 81·5; H, 11·5. $C_{32}H_{54}O_2$ requires C, 81·6; H, 11·6%). The acetate gives a pale yellow coloration with tetranitromethane in chloroform and a yellow colour with the Liebermann–Burchard reagent, the solution exhibiting a green fluorescence which is not so intense as that shown by basseol acetate. The acetate (0·37 g.) was set aside at 0° with a solution of perbenzoic acid in chloroform (100 c.c. of 0·2*N*). From time to time samples of the solution were titrated with 0·1*N*-sodium thiosulphate, all measurements being standardised against a blank consisting of the same volume of perbenzoic acid in chloroform. The following absorptions were observed:

Time (days)	1	2	3	4
Atoms of O absorbed per mole of acetate	0·76	0·89	1·01	1·01

Hydrolysis of bassenyl acetate gives bassenol as an oil. *Bassenyl benzoate* separates from alcohol in laminæ, m. p. 156°, $[\alpha]_D^{19°}$ + 48·1° (*l* = 1, *c* = 1·06 in chloroform) (Found: C, 83·6; H, 10·6. $C_{37}H_{56}O_2$ requires C, 83·4; H, 10·6%).

Ozonolysis of Basseol Acetate.—A slow stream of ozonised oxygen was passed through a suspension of basseol acetate (3·5 g.) in glacial acetic acid (60 c.c.) for 6 hours at room temperature, the issuing gases being bubbled through ice-cold water (100 c.c.). The solutions were mixed, diluted with water (200 c.c.), and distilled in steam until the distillate gave no turbidity with 2 : 4-dinitrophenylhydrazine hydrochloride solution. The distillate was nearly neutralised with sodium carbonate and again distilled in steam. The first fraction (100 c.c.) was boiled for 10 minutes with a solution of dimedon in water; the formaldehyde dimedon derivative (0·4 g., 20%) obtained separated from methyl alcohol in needles, m. p. 187°. The solid residue from the initial steam distillation was extracted with ether and washed with sodium hydroxide solution and water. Removal of the solvent gave a solid, which on crystallisation from methyl alcohol yielded β-amyrenyl acetate oxide in colourless laminæ, m. p. 288°, not depressed by admixture with the β-amyrenyl acetate oxide described by Spring (*loc. cit.*) and giving β-amyrenol oxide, m. p. 200—201°, on hydrolysis with 10% alcoholic potassium hydroxide (Found C, 79·5; H, 10·6. Calc. for $C_{32}H_{52}O_3$: C, 79·3; H, 10·8%).

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The University, Manchester. [*Received, May 15th, 1937.*]

208. *The Mechanism of Hydrolysis and Alcoholysis of Alkyl Halides: The Reactions of Methyl, Ethyl, and* tert.*-Butyl Bromides with Aqueous Ethyl Alcohol.*

By WILLIAM TAYLOR.

ACCORDING to Hughes and Ingold (J., 1935, 249; see also Fig. 1, *ibid.*, p. 238), for the hydrolysis or alcoholysis of alkyl halides, in the series where Alk = Bu^{γ}, Pr^{β}, Et, Me, the velocity of the unimolecular reaction should continuously decrease, and this reaction should in fact be unrealisable or hypothetical for Me and Et. Neither of these deductions, which these authors make from their ionisation theory for such hydrolyses, can be upheld, since it is now found that, not only do both methyl and ethyl bromide suffer the unimolecular reaction in aqueous alcohol, but the velocities are in the order $Bu^{\gamma} \ggg Me > Pr^{\beta} > Et$ (Table I). As this result is not in agreement with their theory, it casts doubt on their

TABLE I.

Values of the first-order velocity coefficients (expressed as min.$^{-1}$ × 10^4) and activation energies (in kg.-cals.).

Solvent (Aqueous EtOH).	MeBr. *k.* 55°.	MeBr. *k.* 25°.	MeBr. *E.*	EtBr. *k.* 55°.	EtBr. *k.* 25°.	EtBr. *E.*	Pr^{β}Br.* *k.* 55°.	Pr^{β}Br.* *k.* 25°.	Pr^{β}Br.* *E.*	Bu^{γ}Br. *k.* 25°.	Bu^{γ}Br. *k.* 15°.	Bu^{γ}Br. *E.*
80%	2·87	0·0733	23·7	1·20	0·0303	23·8	1·42	0·0470	(23·16)	198	61·4	20·0
60%	4·98	0·148	22·8	2·40	0·0605	23·8	4·28	0·158	(22·69)	1920	701	17·2

* Values calculated from the equations of Hughes, Ingold, and Shapiro (J., 1936, 225).

assumption (J., 1935, 251) that the velocities of reaction of hydrogen bromide with the corresponding alkyl acetates in glacial acetic acid, AlkOAc + HBr → AlkBr + HOAc, which are in the order $Bu^{\gamma} \ggg Pr^{\beta} \sim Et < Me$ (Tronov and Sibgatullin, *Ber.*, 1929, **62**, 2850), are to be interpreted by the transformation of a bimolecular mechanism for Me and Et into a mixed uni- and bi-molecular reaction for Pr^{β} and into a unimolecular reaction for Bu^{γ}. The same may be stated for a similar assumption which Hughes and Ingold make on the basis of Tronov and Ladigina's results (*Ber.*, 1929, **62**, 2844) for the reaction of hydrogen bromide with the corresponding phenolic ethers, AlkOPh + HBr → AlkBr + HOPh, in glacial acetic acid. These observations receive support when compared with the velocities of reaction of hydrogen bromide with the corresponding alcohols, AlkOH + HBr → AlkBr + H_2O. Bennett and Reynolds (J., 1935, 131), using phenol as solvent and the approximate molecular ratios of alcohol : hydrogen bromide : water = 1 : 2 : 10, found $Bu^{\gamma} \ggg Me > Pr^{\beta} > Et$. Here the mechanism throughout the series is the same (bimolecular) and hence the minimum velocity reached at Et can certainly not be explained by a change of mechanism. The last reaction is the reverse of the hydrolysis of an alkyl bromide, and the two may be supposed to operate through the same, though reversed, mechanisms (Taylor, this vol., p. 344). In this case the bimolecular nature of the esterification reaction would show that the hydrolysis reaction is also truly bimolecular but simulates a unimolecular nature because of the high proportion of one of the reagents, *viz.*, the solvent water. It is, of course, possible that all these five reactions, which exhibit a similar variation of reaction velocity with a change in the nature of the alkyl radical, hydrolysis and alcoholysis being regarded independently, are bimolecular, and in the author's view the minimum at Et in the series AlkX (X = OAc, OPh, OH, Br) is attributable, not to a break from a uni- to a bi-molecular mechanism, but solely to the varying nature of the group Alk. The reagents—water, alcohol, and hydrogen bromide—must be considered as being similar for these purposes and distinct from basic reagents, for which the relative rates are very different, *viz.*, $Me > Et > Pr^{\beta} > Bu^{\gamma}$ (see, *e.g.*, Hecht, Conrad, and Bruckner, *Z. physikal. Chem.*, 1889, **4**, 288).

EXPERIMENTAL.

Methyl and ethyl bromides were materials of constant b. p. *tert.*-Butyl bromide, prepared by the method of Norris (*Amer. Chem. J.*, 1907, **38**, 641), had b. p. 73—75°/760 mm.

The kinetic experiments were performed with dry, or with 60% and 80% (by vol.) aqueous, ethyl alcohol as solvent media, the alcohol having been dried over and then distilled from lime, followed by refluxing and distillation over calcium. In each experiment 100 c.c. of a solution of the alkyl bromide at the required temperature were taken. The reaction was stopped by adding 10 c.c. of the reaction liquid to benzene (25 c.c.) and water (50 c.c.), and the resulting liquid was titrated with $N/10$-aqueous alkali. The values of the velocity coefficients have been calculated from the equation for a unimolecular reaction: $k = (2\cdot303/t) \cdot \log_{10}a/(a-x)$, a being the concentration of the alkyl bromide in g.-mols./l., and t the time in hours, unless otherwise stated.

Details of representative individual runs are given below, a summary of the results having been given in Table I.

Methyl bromide.

$a = 0\cdot3115$; temp. = 55°; solvent, 80% EtOH.

t	4	10	27	67	117	167	331	1008
NaOH c.c.	2·18	5·06	11·75	21·00	26·90	29·40	31·13	30·90
$k \times 10^4$	174	174	175	167	170	172	—	—

Ethyl bromide.

$a = 0\cdot1240$; temp. = 55°; solvent, 80% EtOH.

t	43	64	91	117	163	422	733
NaOH, c.c.	3·25	4·62	6·03	7·12	8·60	11·80	12·50
$k \times 10^4$	70·7	72·8	73·2	73·0	72·6	71·8	—

Ethyl bromide reacted very slowly indeed with dry ethyl alcohol, and at 55° an "equilibrium" appeared to be established (*i.e.*, titres remained constant) after about 6 weeks, approximately one-sixth of the molecules having apparently reacted. This presumably was due to rate (*b*) equalling rate (*a*) at this, the "equilibrium," concentration.

$$\underset{\text{(solvent)}}{EtBr + HOEt} \longrightarrow EtOEt + HBr \quad . \quad . \quad . \quad . \quad (a)$$

$$\underset{\text{(solvent)}}{HBr + HOEt} \longrightarrow EtBr + H_2O \quad . \quad . \quad . \quad . \quad . \quad (b)$$

(see Taylor, this vol., p. 343).

Methyl bromide also appeared to react relatively slowly with the dry solvent, as the following results show, and probably here again reaction (*b*) was responsible.

Methyl bromide.

$a = 0\cdot4000$; temp. = 55°; solvent, dry EtOH.

t	26	67	117	167	331	655	1008
NaOH, c.c.	3·05	5·28	6·40	7·02	7·98	9·65	10·45

Ethyl bromide.

$a = 0\cdot1240$; temp. = 55°; solvent, dry EtOH.

t	29	70	243	334	658	1011	1512
NaOH, c.c.	0·40	0·84	1·44	1·60	1·75	2·00	2·00

Details of one run with *tert.*-butyl bromide are:

$a = 0\cdot0790$; temp. = 25°; solvent, 60% EtOH.

t (mins.)	1·2	2·0	3·0	4·6	6·5	9·0	15·5	30·0
NaOH, c.c.	1·60	2·60	3·55	4·65	5·60	6·45	7·45	7·85
k (min.$^{-1}$)	0·189	0·199	0·199	0·189	0·190	0·189	0·185	—

It may be taken that these are all substitution reactions, and that little or no olefin is formed. This must be true for methyl bromide. Grant and Hinshelwood (J., 1933, 258) found, and Taylor (J., 1935, 1514) confirmed, that, even with alcoholic potash (approx. $0\cdot1N$), negligible olefin is obtained from ethyl bromide. Hughes (*J. Amer. Chem. Soc.*, 1935, **57**, 708) showed that no propylene is formed from *iso*propyl bromide under the present experimental conditions; and similarly Hughes (J., 1935, 255) obtained no olefin from *tert.*-butyl chloride in aqueous alcohol even up to 45°.

Summary.

The rates of the first-order reactions of methyl, ethyl, and *tert.*-butyl bromides with aqueous ethyl alcohol have been measured, and a mechanism to interpret the results is discussed.

The Polytechnic, Regent Street, London, W. 1. [*Received, March 31st, 1937.*]

209. *The Retardation of Chemical Reactions. Part VII. The Reaction between Potassium Permanganate and Hydrogen Peroxide in Acid Solution.*

By Kenneth C. Bailey and George T. Taylor.

The attention of the senior author was drawn some years ago to the peculiarities of the reaction between potassium permanganate and hydrogen peroxide. During a preparation of the latter compound, he wished to test a distillate qualitatively for peroxide. Sulphuric acid and potassium permanganate were added, but the solution remained purple. Only after ½ hour did decolorisation take place. The same distillate, when diluted with water, decolorised potassium permanganate in acid solution almost instantaneously.

The fact that hydrogen peroxide, in fairly concentrated solution, apparently retards its own reaction with potassium permanganate was already known, and an attempt to elucidate the kinetics of the reaction had been made by Limanowski (*Rocz. Chem.*, 1932, **12**, 519, 638). He used Merck's perhydrol, redistilled it to free it from stabilisers, and followed the course of the reaction colorimetrically, using a green light filter which, being complementary to the red colour of potassium permanganate, increased the accuracy of the reading.

Using only figures for the middle portion of the reaction, and varying the concentrations of his reagents only within narrow limits ($KMnO_4$ 0·0005—0·0015; H_2O_2 0·329—1·12; H_2SO_4 0·0536—0·1072 g.-equiv./l.), he obtained fair agreement with the equation

$$dx/dt = k_1b(1 - x) + k_2ax(1 - x)$$

where x is the fraction of potassium permanganate decolorised (and also the relative concentration of manganous ions, believed to be formed almost instantaneously during the reduction of MnO_4'), and a and b are the initial concentrations of potassium permanganate and hydrogen peroxide.

He found that increase in hydrogen-ion concentration reduced the velocity of the reaction, and was aware that manganous ions promoted the reaction and that hydrogen peroxide in high concentration had an inhibitory effect, which he attributed to the formation of complexes of the type $Mn^{\cdot\cdot},(H_2O_2)_4$, which prevented manganous from interacting with permanganate ions. It is clear that Limanowski's velocity equation makes no provision for a diminution in dx/dt with rise in b, and that, although it may give fair agreement with experimental results over a narrow range, yet it cannot be valid for the reaction in general.

The reaction has been examined more recently by Riesenfeld (*Z. anorg. Chem.*, 1934, **218**, 257), most of whose experimental observations are in good agreement with those of similar experiments by the authors. Taking the time of complete decolorisation as a measure of the velocity of the reaction, he found that, when the concentrations of sulphuric acid and potassium permanganate were constant, and the concentration of hydrogen peroxide was increased gradually from extreme dilution, the velocity of the reaction first rose to a maximum when $[H_2O_2]$ was about 0·005, then fell to a minimum when $[H_2O_2]$ was about 0·5, and then rose slowly at still higher concentrations of hydrogen peroxide. (Concentrations throughout this paper are expressed as g.-equiv./l.) When he used other concentrations of permanganate and acid, the concentrations of hydrogen peroxide at which the velocity was a maximum and a minimum were practically unchanged. In all parts of the curve, an increase in the concentration of permanganate increased the reaction velocity. On the other hand, although an increase in acid concentration increased the velocity in the neighbourhood of the maximum, it retarded the reaction powerfully in the neighbourhood of the minimum.

To explain his results, Riesenfeld suggested that an equilibrium exists in aqueous solution : $2H_2O_2 \rightleftharpoons H_4O_4$. He assumed that at $[H_2O_2] = 0·005$ the peroxide exists almost entirely in unassociated molecules, whereas at $[H_2O_2] = 0·5$ only polymerised molecules are present. The rate of reaction of the polymerised molecules was considered to be very slow compared with that of the simple molecules. The retarding action of sulphuric

acid in the neighbourhood of the minimum velocity was attributed to a stabilising effect on the polymeric molecules.

To this explanation of the retardation at high peroxide concentrations three objections may be offered. (1) Sulphuric acid does not necessarily retard at minimum velocity, as will be clear from an examination of the results which follow. (2) The existence of H_4O_4 is assumed *ad hoc*, and no evidence, such as might be derived from freezing-point determinations, is adduced for the existence of such molecules. (3) Although the *proportion* of polymerised molecules, in an equilibrium such as that postulated by Riesenfeld, would increase with concentration, the *actual number* of simple molecules would also increase in accordance with the equation $[H_4O_4]/[H_2O_2]^2 = K$. Such a hypothesis could not explain a diminution in reaction velocity with increase in concentration, unless a retarding rôle is assigned to H_4O_4, a possibility not envisaged by Riesenfeld.

Experimental.

The hydrogen peroxide was prepared from sodium peroxide and sulphuric acid by the method of Kilpatrick, Reiff, and Rice (*J. Amer. Chem. Soc.* 1926, **48**, 3019), with modifications as recommended by Bailey (*Sci. Proc. Roy. Dublin Soc.* 1935, **21**, 153). As a precaution against decomposition by dust particles at the surface, the pure peroxide solution thus obtained was filtered through three layers of Whatman No. 44 filter-paper into a Pyrex flask which had been washed repeatedly with distilled water similarly filtered (*idem, ibid.*).

Solutions of potassium permanganate were freshly prepared at frequent intervals from recrystallised salt, as comparatively slight decomposition with formation of manganous ions (which catalyse the reaction under investigation) would render the results valueless.

Riesenfeld used the time of complete decolorisation as a measure of the velocity of the reaction, but preliminary experiments showed that this was not legitimate, since in certain cases the time of decolorisation could be varied greatly by altering the rate of stirring (see later). This method of measurement also ruled out experiments with less than the stoicheiometric proportion of hydrogen peroxide. To follow the whole course of an individual reaction by visual colorimetric comparison is possible when the concentrations are so chosen that the reaction is slow, but certainly not when it is complete in 10 or 15 seconds. It was decided therefore to follow the course of the reaction by means of a Lange photo-electric colorimeter. The lamp of the instrument was run off a 100-volt D.C. supply, free from serious fluctuations. The absorption of light by the permanganate solution was recorded continuously on the scale of the instrument, and a preliminary calibration enabled these readings to be converted into concentrations of permanganate. When a green filter was used, the absorption of light by the other substances present was negligible.

It was not found possible to use a constant-temperature room in connection with the 100-volt D.C. supply, but the variation in temperature in any one series of experiments did not exceed 1°. The mean temperatures of the different series are recorded in the appropriate places.

The course of each experiment having been followed from the time of mixing to complete decolorisation, the concentration of permanganate was plotted against time, and the curve produced backwards in order to give the initial velocity (manganous ions being then theoretically absent). As it was difficult to determine the exact slope of the curve at zero time, the velocity of reaction when 82×10^{-7} g.-equiv./l. of permanganate had been reduced was taken as the 'initial velocity.' In all series, this 'initial velocity,' rather than the time of total decolorisation, has been regarded as significant, and used in the curves given.

The chief practical difficulty is due to the fact that even the slightest decomposition of the permanganate solution (*e.g.*, by reducing agents in dust) is likely to produce some manganous ions, which are therefore almost certainly present in minute but variable concentration at the outset in all experiments. This difficulty has not been completely overcome, and inconsistencies, probably due to this source, have been observed between different series of experiments.

Effect of Stirring on Reaction Velocity.—This effect is illustrated by Fig. 1. Solutions *a*, *b*, and *c* all contained the same concentrations of hydrogen peroxide (0·098), sulphuric acid (0·05), and potassium permanganate (0·00057). The early parts of the three curves really coincide, but curves *b* and *c* have been displaced in the figure for clearness. The times of total decolorisation were:

a (no stirring after initial mixing)	300 secs.
b (intermittent gentle stirring)	655 secs.
c (continuous vigorous stirring)	695 secs.

In Table I, S = speed of stirring (r.p.m.), T = time for complete decolorisation (secs.), $[KMnO_4] = 0·0005$, $[H_2SO_4] = 0·025$.

TABLE I.

$[H_2O_2]$	0·0005.		0·00075.		0·00125.		0·0312.		0·044.		0·062.	
	S.	*T.*	*S.*	*T.*	*S.*	*T.*	*S.*	*T.*	*S.*	*T.*	*S.*	*T.*
	95	23·6	76	15·5	100	10·0	68	10·5	50	14·5	86	33·6
	143	24·8	93	15·9	120	10·8	107	10·8	78	14·0	109	33·0
	171	23·6	120	16·5	150	11·6	133	10·4	102	13·6	133	33·0
	198	23·2	150	17·0	200	12·6	150	10·1	143	15·7	158	40·6
	286	24·6	200	16·0	286	12·8	182	11·5	194	23·5	193	160
	400	25·2	273	16·6	400	12·0	264	17·8	222	21·5	214	240
	492	23·1	344	16·9			364	18·8	361	47·4	353	370
			392	15·4			476	25·3	458	60·8		

It will be seen that at low concentrations of hydrogen peroxide, the speed of stirring has little effect, but that at high concentrations its effect is very considerable. We are probably concerned here with the catalytic action of manganous ions. At low concentrations of peroxide, these

FIG. 1.

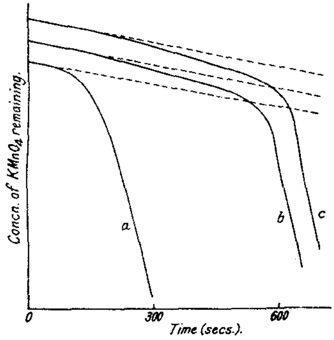
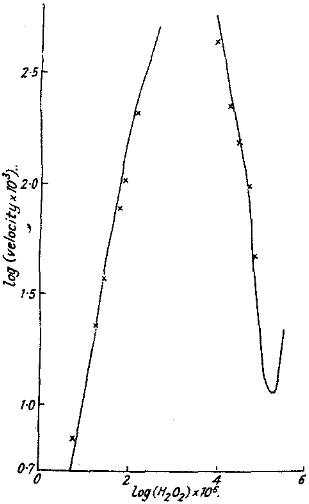


FIG. 2.



ions are very efficient catalysts, while at high concentrations they have comparatively little effect. In the latter case, their effect may be enhanced if they are allowed to accumulate locally, a theory supported by the streakiness often visible during the decolorisation of an unstirred solution. Stirring would prevent such local accumulation and thus retard the reaction. At peroxide concentrations in the neighbourhood of the velocity maximum, the later stages of decolorisation are in all events so rapid that changes due to local accumulation of catalyst would be obscured.

In all the experiments which follow, the reaction mixture was kept vigorously stirred except when readings were being taken.

Series A (15°): $[KMnO_4] = 0·0005$; $[H_2SO_4] = 0·025$; $[H_2O_2]$ *variable.* A curve was obtained (Fig. 2) similar to that of Riesenfeld. The maximum and the minimum velocity were

at $[H_2O_2]$ = *ca.* 0·005 and 0·16 respectively. The velocities in the neighbourhood of the maximum were too great for the course of the reaction to be followed, even with the photoelectric colorimeter. The stoicheiometric concentration of hydrogen peroxide is 0·0005, which does not correspond with the maximum velocity. In Figs. 2 and 4, the logarithms of the velocity and of the concentration of hydrogen peroxide (or sulphuric acid) have been used for convenience in plotting.

Series B (16°), *C* (18°), *D* (15°), *and E* (19°): $[KMnO_4]$ = 0·0005; $[H_2O_2]$ = 0·0000154 (B), 0·000028 (C), 0·00004 (D), 0·00075 (E); $[H_2SO_4]$ *variable in all series.* The concentrations of hydrogen peroxide in all these experiments were lower than that corresponding with the maximum velocity. It will be seen (Fig. 3) that increase in concentration of acid increases reaction velocity in all four series, but that there is a tendency, especially noticeable in B and C, for the reaction velocity to become independent of the concentration of acid, when large amounts of the latter are added.

FIG. 3.

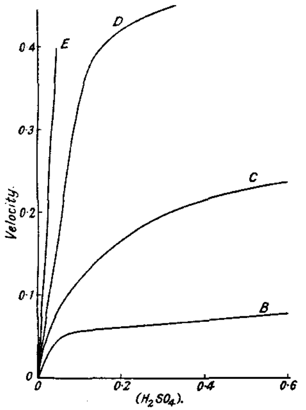
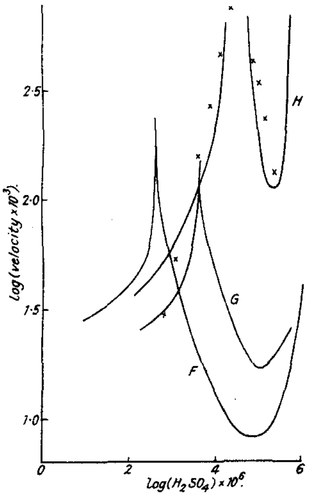


FIG. 4.



Series F (21°), *G* (15°), *and H* (16°): $[KMnO_4]$ = 0·0005; $[H_2O_2]$ = 0·100 (F), 0·049 (G), 0·0285 (H); $[H_2SO_4]$ *variable in all series.* Here we are dealing with concentrations of hydrogen peroxide higher than that corresponding with the maximum velocity, and we find that variation in acid concentration yields a curve of entirely different type (Fig. 4) from those obtained in Series B, C, D, and E. Each curve shows a very sharp maximum, and a well-defined minimum.

Series I (18°), *J* (17°), *and K* (18°): $[H_2SO_4]$ = 0·025; $[H_2O_2]$ = 0·042 (I), 0·065 (J), 0·00096 (K); $[KMnO_4]$ *variable in all series.* Whether the concentration of hydrogen peroxide is less (as in K) or greater (as in I and J) than that corresponding with the maximum velocity, the reaction velocity increases with permanganate concentration (Fig. 5).

Series L (15°). Limanowski's observation that moderate acceleration is produced by glass surfaces, at low concentrations of hydrogen peroxide and sulphuric acid, was confirmed. Using 100 c.c. of the reaction mixture, $[KMnO_4]$ = 0·0005, $[H_2SO_4]$ = 0·025, $[H_2O_2]$ = 0·0005 or 0·00073, we observed increases in reaction velocity of 9 and 22% respectively, when 230 sq. cm. of glass surface, in the form of short glass rods, were introduced.

Discussion.

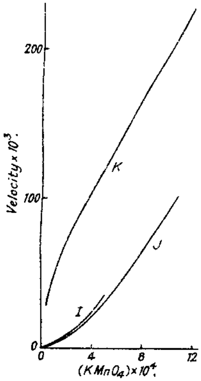
A satisfactory theory of the reaction must explain the following facts, a few of which were known before 1932, the remainder having been established by Limanowski, Riesenfeld, and the authors.

(i) When initial [$KMnO_4$] and [H_2SO_4] are constant, and initial [H_2O_2] is gradually increased, the reaction velocity increases to a maximum at [H_2O_2] = 0·005, falls to a minimum at [H_2O_2] = 0·16, and rises slowly at still higher [H_2O_2].

(ii) When initial [$KMnO_4$] and [H_2O_2] are constant, and the latter low (less than 0·001), the velocity increases with increase in [H_2SO_4] and shows some tendency to become constant at high [H_2SO_4].

(iii) When initial [$KMnO_4$] and [H_2O_2] are constant, and the latter high (greater than 0·02), the velocity rises to a maximum (the position of which varies with [H_2O_2]) as [H_2SO_4] increases, then falls to a minimum, and finally rises again at high [H_2SO_4].

Fig. 5.



(iv) Manganous ions catalyse the reaction powerfully at concentrations of hydrogen peroxide smaller than and up to that corresponding with maximum velocity, but have comparatively little effect at concentrations of hydrogen peroxide in the neighbourhood of the minimum velocity.

(v) The velocity increases with, but (at least at high peroxide concentrations) not in direct proportion to, permanganate concentration.

The theories of Limanowski and Riesenfeld are incapable of explaining all these facts, but we, too, are unable to advance a theory which is free from objections. It is difficult to formulate any single mechanism which will account for *both* maximum and minimum in the curve of Fig. 2 or in those of Fig. 4, and it seems probable that the rise in velocity at high [H_2O_2] is due to a secondary reaction, the velocity of which is negligibly small when [H_2O_2] is less than 0·1. One is tempted to suppose that the rise in velocity at high concentrations of acid (Fig. 4) must be attributed to the same secondary reaction. It will be noticed, however, that the concentrations of peroxide in curves G and H are less than that at which the secondary reaction has been assumed to vanish, and no obvious explanation is forthcoming.

If we assume the intervention of a secondary reaction at [H_2O_2] greater than 0·1, we have still to account for a reaction, the velocity of which rises to a maximum at [H_2O_2] = 0·005, becomes negligibly small at [H_2O_2] = *ca.* 0·2, and is affected by changes in the concentration of acid, permanganate, and manganous ions as set forth above.

The curves of Figs. 2 and 4 bear some resemblance to those obtained for chain reactions which are explosive between certain limits of pressure and non-explosive outside them (see, *e.g.*, Fig. 2 of Thompson and Hinshelwood, *Proc. Roy. Soc.*, 1929, *A*, **122**, 610). It is possible, therefore, that we have to do with a chain reaction, but we believe that the explanation may lie in another direction.

Hydrogen peroxide is one of the few chemical compounds which are both reducing and oxidising agents. The ordinary reaction with potassium permanganate in acid solution may be considered as a reduction of the permanganate:

$$2MnO_4' + 5H_2O_2 + 6H^{\cdot} = 2Mn^{\cdot\cdot} + 8H_2O + 5O_2.$$

It is very unlikely that the reduction of MnO_4' to $Mn^{\cdot\cdot}$ really takes place in one step; if we suppose that it takes place in stages, the first stage may involve the production of an ion such as MnO_3', which might be capable of being reoxidised to MnO_4' by a hydrogen peroxide molecule with sufficient energy. The likelihood of such reoxidation would increase with rise in [H_2O_2].

A fair agreement with experiment may be obtained by using the empirical equation

$$v = k_1[H_2O_2][H_2SO_4][KMnO_4]/(k_2 + k_3[H_2O_2]^2[H_2SO_4]^2) \quad . \quad . \quad . \quad (1)$$

The term in the numerator represents the promotion of the reaction, while the terms in the denominator represent two types of retardation, the second, on our theory, being the reoxidation of the partially reduced permanganate by active hydrogen peroxide. Equation (1) reduces to

$$v = k_1[H_2O_2][H_2SO_4][KMnO_4]/k_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$

at very low peroxide concentrations (Fig. 3, and the left-hand sides of the curves in Figs. 2 and 4), and to

$$v = k_1[KMnO_4]/k_3[H_2O_2][H_2SO_4] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

at high peroxide concentrations, unless k_2 also is large (the descending portions of the curves in Figs. 2 and 4).

Equation (1) ignores the catalytic effect of manganous ions. If, however, we suppose that the reaction represented by the term in the numerator, and the retardation represented by the second term in the denominator, are both catalysed by manganous ions, the effect of these ions will be great at low peroxide concentrations, and possibly very small at peroxide concentrations high enough for the second term in the denominator to become predominant.

Curves drawn with the aid of equation (1) can be made to correspond fairly closely with those of Figs. 1—5. For example, the crosses in Fig. 2 represent points obtained by giving k_1, k_2, and k_3 the values 1, 10^{-8}, and 5 respectively, while in plotting those in Fig. 4 (curve H) the values 3·75, 10^{-8}, and 2 were used.

The fact that different values must be assumed for the constants before the different curves can be reproduced may be due to slightly different concentrations of manganous ions initially present in the different series of experiments, but probably indicates that the equation requires modification.

We are unable to propose any detailed mechanism, to which exception might not properly be taken, for this very complicated reaction.

The authors' thanks are due to Mr. T. N. Richardson and Mr. C. W. Grove-White, who carried out some preliminary experiments on this reaction.

TRINITY COLLEGE, DUBLIN. *[Received, May 7th, 1937.]*

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210. *Long-chain Carbon Compounds.* n-*Tetratriacontanoic and* n-*Hexatetracontanoic Acids and their Derivatives.*

By FRANCIS FRANCIS, A. MILLICENT KING, and JOHN A. V. WILLIS.

THE crystal spacings of the synthetic higher *n*-fatty acids and many of their derivatives, together with the heats of crystallisation of a series of their ethyl esters, have been examined in these laboratories (for the former, see *Proc. Roy. Soc.*, 1930, *A*, **128**, 24; 1937, *A*, **158**, 691; and for the latter, J., 1934, 1449; 1936, 1372). For this purpose, preparations of the highest attainable degree of purity were necessary.

The pure *n*-aliphatic acids dissolve in concentrated sulphuric acid at 70°, giving colourless solutions; on the other hand, the purest specimens of myristic, palmitic and stearic acids obtained from Schering–Kahlbaum all give dark solutions owing to the presence of unsaturated material, which may be oleic acid. Myristic acid can be completely freed from this impurity by two crystallisations from glacial acetic acid, palmitic acid by four, but after this operation has been repeated six times, stearic acid still shows the presence of oleic acid. The most satisfactory method of eliminating this substance from palmitic and stearic acids consists in a preliminary crystallisation from concentrated sulphuric acid, the temperature of which must not be raised above 70°, followed by three from acetic acid. For this purpose, it is essential that anhydrous acetic acid should be used.

Each of the three acids then contains quantities of the order of 1% of, presumably, lower or higher homologues, and the final purification is effected by converting them into their ethyl esters, fractionating these in a vacuum, and reconverting the middle fraction into the acids, which are then recrystallised from acetic acid until their respective setting points are constant to within $\pm$ 0·01°. The m. p. determined in a capillary tube by the ordinary method is of very much less value as a criterion of purity, although a more accurate observation can be made, and a better judgment formed of the purity of the specimen, by using the apparatus previously described (J., 1936, 137). In this, the temperature at which resolidification takes place has never been found to differ by more than $\pm$ 0·2° from the setting point.

If an alcoholic solution of an alkali is used for the saponification of the esters, it is advisable in all cases to remove the alcohol before the soaps are decomposed by a mineral acid, for experience has shown that there is a possibility of the resulting organic acids being contaminated with re-formed esters unless this precaution is taken.

The acids of even, and in some cases, odd, carbon content higher than 22 were obtained from behenic acid, which can be prepared from erucic acid in an exceptionally pure condition. The synthesis of the acids of *even* carbon content, commencing with 110 g. of behenic acid, can be continued up to *tetratriacontanoic acid*, but an insufficient amount (4—5 g.) of that acid is obtained for further progress. The following well-known methods were employed : reduction of the ethyl esters to the corresponding alcohols, the conversion of these into iodides, and then into malonic ester derivatives, and the decomposition by heat of the dicarboxylic acids. Acids with an *odd* number of carbon atoms were prepared from the iodides by interaction with potassium cyanide and the hydrolysis of the resulting nitriles.

In the various operations, loss of material is due mainly to the precautions necessary for the purification of all the intermediate derivatives. For instance, one must fractionate the esters in a high vacuum before proceeding to the synthesis of the next higher acid, or determining their heats of crystallisation, or converting them into acids for crystallographic work. This procedure has also to be followed in the case of alcohols, prepared by the reduction of the esters by the Bouveault–Blanc method, for these derivatives cannot be freed from small quantities of sodium salts by crystallisation alone. Dicarboxylic acids cannot be completely decomposed into monocarboxylic acids unless quantities not greater than 6 g. are taken, and they must be maintained in a fused condition for long periods in a high vacuum. Finally, the sharpness of the melting points of the respective α- and β-modifications of the iodides containing 22 to 30 carbon atoms constitutes a valuable criterion of their purity. Beyond C_{30} these derivatives appear to exist in the α-form only.

A further quantity of tetratriacontanoic acid was prepared by following the method used by Mrs. G. M. Robinson for the synthesis of triacontanoic acid (J., 1934, 1544). Both the acid and its *ethyl* ester were identical in all respects with those obtained stepwise from behenic acid; this is a valuable confirmation of the purity of the acid, since the possible impurities would not be identical in both preparations.

From the acid containing 34 carbon atoms, those with 36 and 38 were prepared, but the most interesting was that with 46 atoms synthesised by the Robinson method. Also, from the first of these acids small quantities of the *α-hydroxy-acid*, and the *hydrocarbons* containing 66 and 67 carbon atoms, were obtained, although in insufficient amount to effect satisfactory purification. The crystal spacing of the former hydrocarbon varied by + 0·5%, and the latter by + 1·0% from the *A* values calculated by extrapolation from those of lower carbon content. These two hydrocarbons, the acids mentioned above, and the α-hydroxy-acid contain a larger number of carbon atoms than any whose spacings have yet been determined.

Crystals of acids containing an even number of carbon atoms obtained by deposition from such non-polar solvents as acetone or benzene show the *B* crystal spacings, whereas from acetic acid they give the *C* spacing only. On the other hand, the crystals of acids containing an odd number of carbon atoms show the *B* spacings irrespective of the solvent used in their preparation.

When both the *B* and the *C* spacings are plotted against the carbon content of the even-membered acids, straight lines are obtained on which lie with striking accuracy the spacings of all such acids up to that containing 46 atoms. A similar relationship is shown

by the ethyl esters, alcohols, iodides, and dicarboxylic acids, and by the acids of odd carbon content.

The heats of crystallisation of the methyl and ethyl esters of many of these acids have been described previously and that of ethyl tetratriacontanoate is given in this communication.

EXPERIMENTAL.

n-*Tetratriacontanoic Acid*.—This was prepared in the first instance by following in detail the method used by Mrs. G. M. Robinson (*loc. cit.*) to synthesise the acid containing 30 carbon atoms.

The most suitable method for the preparation of behenoyl chloride consists in the action of oxalyl chloride on a benzene solution of behenic acid. It is purified by distillation in a vacuum of 10^{-5} mm., melts at 40°, is very soluble in ether or benzene, and rapidly hydrolysed when exposed to the air (Found: Cl, 9·6. Calc. for $C_{22}H_{43}OCl$: Cl, 9·9%).

This chloride was allowed to react with ethyl sodio-α-acetylbrassylate, ether being used as a medium in some preparations and benzene in others without affecting the final yield. The product, ethyl α-acetyl-α-behenoylbrassylate, was saponified in three stages, (1) shaking with cold 3% aqueous caustic soda, (2) boiling with 5% sulphuric acid, and (3) refluxing with 8% aqueous soda. The final yield of 13-ketotetratriacontanoic acid was unaffected if treatment (2) was omitted, or if the final saponification was carried out at a lower temperature, or with a higher or lower concentration of alkali. The products of the saponification formed an insoluble cake consisting of the sodium salts of behenic acid with much smaller quantities of 13-ketotetratriacontanoic acid, and some 12-acetyl-lauric acid. The mixture was converted into the free acids, which were repeatedly ground with small quantities of alcohol to remove the 12-acetyl-lauric acid and some behenic acid, and the residual acids were esterified with ethyl alcohol. The crystalline esters were repeatedly washed with large quantities of cold ether, in which ethyl behenate alone was soluble, and the residual keto-ester purified by several crystallisations from benzene.

From six preparations, some of which were carried out by Dr. F. J. E. Collins, a total amount of 50 g. of the pure keto-ester was obtained. This represents an average yield of 14%, and the behenic acid recovered, 70%, calculated on the behenic acid used as behenoyl chloride in the synthesis.

Considerable quantities of 12-acetyl-lauric acid were isolated both from the alkaline solutions used in the saponification and during the operations mentioned above.

Ethyl 13-*ketotetratriacontanoate*, m. p. 80·9°, r. p. 80·2°, is only slightly soluble in boiling ether (Found: C, 78·4; H, 12·5. $C_{36}H_{70}O_3$ requires C, 78·5; H, 12·7%). The *acid* itself has m. p. 107·7° and gives a crystal spacing of 90·9 A. (Found: C, 78·2; H, 12·5. $C_{34}H_{66}O_3$ requires C, 78·1; H, 12·6%).

12-*Acetyl-lauric acid*, crystallised from acetone, has m. p. 73·5° and its crystal spacing is 39·63 A. (Found: C, 69·4; H, 10·7. $C_{14}H_{26}O_3$ requires C, 69·4; H, 10·7%). On oxidation with sodium hypobromite it gives a nearly quantitative yield of brassylic acid, m. p. 113·3° (Found: C, 63·8; H, 9·8. Calc. for $C_{13}H_{24}O_4$: C, 63·9; H, 9·8%).

n-*Tetratriacontanoic acid* was obtained in 80% yield by the reduction of the keto-acid by Clemmensen's method, the course of the reaction being followed by observations of the m. p. of the product, which fell during the operation from 107·7° to about 94°; after it had risen to 96·1°, the reduction was complete. The acid was purified by conversion into the ethyl ester, which was distilled in a vacuum of 10^{-5} mm. and on saponification gave the free acid, m. p. 98·2°, r. p. 97·8°, and s. p. 98·0°. The solubility of the acid in boiling ether or methyl alcohol is about 0·04% in each case (Found: C, 80·2; H, 13·6. $C_{34}H_{68}O_2$ requires C, 80·3; H, 13·4%). The potassium salt is almost insoluble in water or boiling benzene, and soluble to the extent of about 0·15% in boiling ethyl alcohol.

The *ethyl* ester of this acid has a setting point of 75·3°, m. p. 75·4°, r. p. 75·2° (Found: C, 80·5; H, 13·5. $C_{36}H_{72}O_2$ requires C, 80·6; H, 13·4%). The *anilide*, prepared by the interaction of tetratriacontanoyl chloride and aniline in benzene solution, has m. p. 114°, r. p. 113° (Found: N, 2·7. $C_{40}H_{73}ON$ requires N, 2·4%).

α-*Bromotetratriacontanoic acid* was prepared from the acid by Hell and Sadomsky's method (*Ber.*, 1891, **24**, 2388). It is soluble in ether and may be crystallised from benzene (Found: Br, 13·7. $C_{34}H_{67}O_2Br$ requires Br, 13·6%). This acid shows a type of dimorphism very similar to that observed in some of the higher *n*-aliphatic iodides. The β-modification is formed by allowing a specimen to remain at room temperature for some time. It melts at 89·1° and if

the temperature is allowed to fall slowly it resolidifies at 87° and on again heating shows the same m. p. If the specimen in the capillary tube, however, is heated to 96° and then allowed to cool, resolidification takes place at 76·5° and if the temperature is raised at once, the α-modification formed under these conditions melts at 77·37°.

The corresponding *α-hydroxy-acid* was prepared from the bromo-derivative by the method described by Ashton, Robinson, and Smith (J., 1936, 285). When a solution in acetone, acetic acid or benzene is cooled rapidly, it separates as a gel, although ill-defined crystals can be obtained by slowly cooling a benzene solution. These crystals melt indefinitely at 109°, although after resolidification they re-melt at about 102°, and Dr. Piper found the crystal spacing to be 87·6 A., calculated from a poor photograph. This value falls on the extrapolation of the *A* graph connecting the spacings of the lower α-hydroxy-acids with their carbon content. Since the synthetic acids give the *B* spacings, Dr. Piper considered that the specimen was impure. An attempt was made to purify the small amount available by recrystallisation of its ethyl ester, which was afterwards converted into the barium salt of the acid. This salt was then extracted with boiling acetone, followed by benzene, to remove any inert material that might have been present. The acid recovered from the salt was similar in its behaviour to the original specimen. On crystallisation from benzene it fused indefinitely between 109° and 110°, but on resolidifying it remelted at about 104—105°. The crystal spacing, however, was now 77·0 A., calculated from a better photograph than the first, and this lies on the extrapolation of the *B* graph (Found: C, 77·5; H, 12·9. $C_{34}H_{68}O_3$ requires C, 77·8; H, 13·0%).

Tetratriacontanoyl chloride was obtained by the action of oxalyl chloride on the acid in benzene solution. Recrystallised from this solvent, it had m. p. 73·1°, r. p. 72·8°. It was slowly hydrolysed when exposed to the air in the crystalline condition (Found: Cl, 6·7. $C_{34}H_{67}OCl$ requires Cl, 6·7%).

n-*Hexahexacontane*.—This *hydrocarbon* was prepared by the electrolysis of potassium tetratriacontanoate, but owing to its small solubility in aqueous alcohol at 70° it was only possible to deal with small quantities at a time. The products from several experiments were combined, the unchanged organic acid removed by boiling alcohol, and the hydrocarbon purified by repeated treatment with hot sulphuric acid until blackening no longer took place. It is insoluble in alcohol and may be recrystallised from benzene; m. p. 103·6°, r. p. 103·3°. The crystal spacing, 85·47 A., corresponds to the *A* form of the hydrocarbon, but this value shows that probably it was not pure (Found: C, 85·6; H, 14·3. $C_{66}H_{134}$ requires C, 85·5; H, 14·5%).

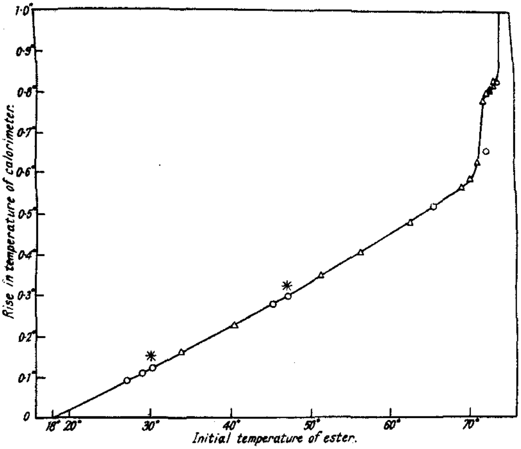
n-*Heptahexacontan*-34-*one* was prepared in small yield by the method described by Easterfield and Taylor (J., 1911, 99, 2298); m. p. 109—110° [Found: C, 84·2; H, 13·7. $(C_{33}H_{67})_2CO$ requires C, 84·3; H, 14·0%]. When this was reduced by Clemmensen's method, it gave *heptahexacontane*, which was purified as described above. It is insoluble in alcohol and may be recrystallised from benzene; m. p. 104·1°, r. p. 103·9°. Its crystal spacing, 87·84 A., calculated from a poor photograph, showed that the specimen was impure (Found: C, 85·3; H, 14·2. $C_{67}H_{136}$ requires C, 85·5; H, 14·5%).

Heat of Crystallisation of Ethyl Tetratriacontanoate.—The measurements were carried out in identical apparatus and in an exactly similar manner to those described for the lower members of the series (King and Garner, J., 1936, 1372). As before, only the data essential for the calculation of the specific heats and heats of crystallisation are given (Table I), but the complete experimental data (below the setting point) are plotted in the figure, in which points marked △ again represent experiments in which the molten ester was allowed to crystallise in the thermostat at the temperature of the experiment, and those marked ⊙, experiments in which the ester was solid when it was placed in the thermostat. The water equivalent of the calorimeter was 338·8.

From the figure it appears that the curve for the tilted form may be divided into three straight portions, and that the breaks occur at 30° and 47° (*) corresponding to the transition temperatures of one tilted form into another, *i.e.*, $\beta_1 \longrightarrow \beta_2$ and $\beta_2 \longrightarrow \beta_3$ respectively. These transitions are reversible. The figure also shows that the transition from the vertical to the tilted form is completely reversible, confirming the view expressed by King and Garner (*loc. cit.*) that the vertical chains are more stable than the tilted chains at the melting point for compounds with very long chains. The transition temperature is approximately 3° below the setting point.

If the straight line drawn through the values of Q_V for the lower members of the series be extrapolated to C_{34}, a value of 21 kg.-cals./g.-mol. is obtained. Experimentally, Q_V was found to be abnormally low, *viz.*, 19·75 kg.-cals./g.-mol., a result which may be due either to the presence of impurity or to a factor which enters only into the crystallisation of the higher members of the series, causing divergence from the predicted values. A second abnormality

occurs in the specific heat of the vertical form of the C_{34} ethyl ester, which is 1·24 cals./g., as compared with the mean value, 0·71 cal./g., for the members up to and including C_{30}. It must be pointed out, however, that, since the vertical form is only stable over a range of 3° below the



setting point, the accuracy of measurement is not as great as in the lower members of the series where measurements of the vertical form may be carried out over a greater range of temperature.

Acids of Carbon Content higher than 34.—Dr. F. J. E. Collins prepared in these laboratories n-*hexatriacontanoic acid* from *n*-tetratriacontanoic acid, and n-*octatriacontanoic acid* from the former acid, by the methods previously mentioned. *n*-Hexatriacontanoic acid had m. p.

TABLE I.

Ethyl tetratriacontanoate (setting point = 75·19°).

(Wt. of ester, 5·0519 g.; glass, 5·6715 g.; platinum, 0·1428 g.)

Expt. No.	Initial temp. of ester.	Fall in temp.	Rise in temp.	Expt. No.	Initial temp. of ester.	Fall in temp.	Rise in temp.
1	29·11°	11·64°	0·113$_8$	21	47·26°	29·22°	0·2951°
29	72·61	54·89	0·800$_7$	27	65·64	48·13	0·524$_3$
31	73·96	55·95	0·827$_7$	24—26	95·73	78·09	1·648$_8$
5	30·34	12·69	0·123$_1$	20, 22, 23	80·43	62·80	1·468$_3$
14	45·35	27·60	0·277$_8$				

σ_{ST_1} = 0·4344 cal./g.; σ_{ST_2} = 0·4709 cal./g.; σ_{ST_3} = 0·5860 cal./g.
σ_{SV} = 1·242 cal./g.; σ_L = 0·5520 cal./g.
Q_{T_1} = 30·48 kg.-cals./g.-mol. Q_V = 19·75 kg.-cals./g.-mol.
Heat of transition V ⟶ T_1 = 10·73 kg.-cals./g.-mol.

99·9°, r. p., 99·4° (Found: C, 80·4; H, 13·3. $C_{36}H_{72}O_2$ requires C, 80·6; H, 13·4%), its ethyl ester m. p. 78·6°, r. p. 78·3°, and the corresponding *alcohol* m. p. 92·9°, r. p. 92·1° (Found: C, 82·55; H, 14·1. $C_{36}H_{74}O$ requires C, 82·7; H, 14·2%). *n*-Octatriacontanoic acid had m. p. 101·6°, r. p. 100·1° (Found: C, 80·6; H, 13·4. $C_{38}H_{76}O_2$ requires C, 80·8; H, 13·5%), and its *ethyl* ester m. p. 80·55°, r. p. 80·3° (Found: C, 81·3; H, 13·4. $C_{40}H_{80}O_2$ requires C, 81·1; H, 13·5%). The corresponding *alcohol* was obtained in insufficient quantity to enable it to be purified satisfactorily. A condensate from the molecular still had m. p. 93·6° (Found: C, 82·6; H, 14·0. $C_{38}H_{78}O$ requires C, 82·9; H, 14·2%).

13-*Ketohexatetracontanoic Acid.*—This was prepared by the Robinson method. Tetratriacontanoyl chloride (15 g.) was allowed to react in ethereal solution in an atmosphere of nitrogen with a slight excess of ethyl sodio-α-acetylbrassylate. The resulting derivative, extracted in the usual manner, was shaken for 10 hours with a cold aqueous solution of potassium hydroxide. When the insoluble material was dissolved in ether, 4 g. of potassium tetratriacontanoate, probably due to the incomplete interaction of the acid chloride and the sodio-derivative, remained behind. The ethereal solution was evaporated and left 11·8 g., which were recrystallised from alcohol, and although an indefinite m. p. of 68—90° showed that it was not pure, the analytical data are close to those required for *ethyl α-acetyl-α-tetratriacontanoylbrassylate* (Found : C, 76·6; H, 12·0. $C_{53}H_{100}O_6$ requires C, 76·4; H, 12·0%). This derivative was unaffected by boiling with 8% aqueous potassium hydroxide, and saponification was effected in alcoholic solution. The solid potassium salts that separated were washed with water to remove potassium 12-acetyllaurate, converted into acids, and esterified with ethyl alcohol. The mixture of esters was distilled in a vacuum of 10^{-5} mm.; the distillate, constituting the main bulk of the product, was ethyl tetratriacontanoate, s. p. 75·30°. The residue in the flask was nearly pure *ethyl* 13-*ketohexatetracontanoate*, m. p. 91·7°. After several recrystallisations from benzene, the m. p. was 93·76° (Found : C, 80·05; H, 13·1. $C_{48}H_{94}O_3$ requires C, 80·2; H, 13·1%). The amount of pure ester was 1·5 g.; the yield, calculated as before, was equivalent to about one half of that obtained in the synthesis of the corresponding ketone containing 34 carbon atoms. It could not be raised by carrying out the saponification with barium hydroxide in place of potassium hydroxide. After several preparations, about 4 g. were finally obtained. The *acid* itself, m. p. 115°, had a crystal spacing of 124·0 A. (Found : C, 80·0; H, 12·9. $C_{46}H_{90}O_3$ requires C, 80·0; H, 13·0%).

Hexatetracontanoic acid was prepared in 86% yield by the reduction of the keto-acid by Clemmensen's method; m. p. 107·1° (Found : C, 81·6; H, 13·7. $C_{46}H_{92}O_2$ requires C, 81·7; H, 13·6%). The *ethyl* ester had m. p. 90·5°, r. p. 90·3°; the purity of the preparation was tested by taking two condensates in the molecular still, the first with the bath at 130° and the second at 150°. Both the original specimen and the first and second fractions all melted at the same temperature, *viz.*, that given above (Found : C, 81·6; H, 13·6. $C_{48}H_{96}O_2$ requires C, 81·8; H, 13·6%).

THE UNIVERSITY, BRISTOL. [*Received, March 19th*, 1937.]

211. *Catalytic Toxicity and Chemical Structure. Part II. The Influence of Chain Length in the Alkyl Sulphide and Thiol Series.*

By EDWARD B. MAXTED and HERBERT C. EVANS.

IN a previous paper (this vol., p. 603), the relative toxicity of a number of sulphur compounds towards platinum and nickel hydrogenation catalysts was examined. It was found that, in general, the toxicity per unit of sulphur increases with the complexity of the inhibiting molecule of which the sulphur forms part, even if the remainder of this molecule contains no elements or groups which normally act as catalyst poisons; and the effect of the permanent attachment, at one point, of a complex molecule containing—in addition to a poisonous element or group responsible for the permanent linkage—a normally non-toxic chain or ring was discussed. It was pointed out that, even if the structure of the residual chain were such that—in the absence of the anchor effect introduced by the presence of the poisonous element proper—it would be freely adsorbed and evaporated from the catalytic surface, it should, by virtue of its permanent proximity to the surface, be in a preferential position for further attachment and thus, as a result of this preferential adsorption, it might act as if it were itself toxic.

The subject has now been examined more systematically by measuring the increase in toxicity induced by the attachment to a sulphur atom of simple chains of known length; and this paper relates to relative toxicities in the alkyl sulphide and alkyl thiol series towards platinum in catalytic hydrogenation. It was found that the molecular toxicity—*viz.*, the toxicity expressed, as before, per g.-mol. of inhibitant or per unit mass of sulphur—increases, within both series of poisons, continuously with the chain length. The rate of

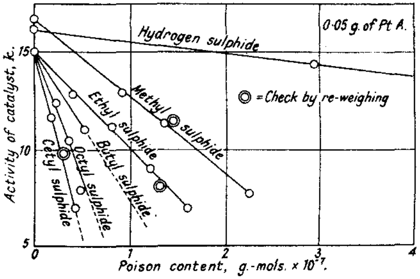
increase in toxicity with each additional chain unit decreases, however, as the length of the chain becomes greater. This would be expected from the gradual recession of the anchor effect.

If poisoning is assumed to be caused by the obstructive coverage of potentially active surface, the increase in toxicity or covering power brought about by the attachment to sulphur of a chain of known length, and consequently of known maximum range of action, is of great interest in connection with the existence of special catalytically active points in the surface, since it allows an estimate to be made of the distance separating catalytically active surface elements and the comparison of this distance with that between the normal elements of the surface lattice. This point is dealt with in greater detail later. In view of the effect of even short chains on the toxicity, these distances are apparently identical; and it consequently seems probable that all surface elements can act catalytically. This homogeneity of a metallic catalysing surface is in agreement with evidence put forward from other standpoints (J., **1933**, 502; **1934**, 26, 672; **1935**, 393).

EXPERIMENTAL.

The procedure employed in measuring toxicity was as described in the previous paper, to which reference should be made. In the case of each inhibitant, the activity of the catalyst at various known stages of poisoning was plotted against the poison content; and, from the slope

FIG. 1.



of the poisoning graph, the poisoning coefficient, α, which is a measure of the toxicity, was calculated by means of the relationship $k_c = k_0(1 - \alpha c)$, in which k_c is the activity of the catalyst in the presence of a quantity, c, of the poison, and k_0 is its original, unpoisoned activity. As before, the rate of hydrogenation of crotonic acid in acetic acid solution was employed as a convenient standard hydrogenation reaction for the measurement of the catalytic activity, and platinum was taken as the catalyst throughout. A sufficient stock of the same standard preparation of platinum-black as had been used in the measurements previously described remained available for use throughout the alkyl sulphide series. For the measurements involving alkyl thiols, a fresh stock of platinum-black was prepared. These two standard preparations are indicated, respectively, by Platinum A and Platinum B. The system taken for hydrogenation in each case consisted, as before, of 0·05 g. of platinum, 10 c.c. of a *N*-solution of crotonic acid in glacial acetic acid, and the known quantity of poison dissolved in a further 10 c.c. of acetic acid, hydrogenation being carried out in a mechanically shaken reaction pipette, at 27°, with the previously described precautions for the standardisation of conditions.

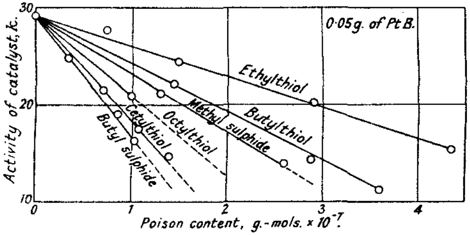
Relative Toxicity of the n-*Alkyl Sulphides.*—As representative sulphides of various chain lengths, methyl, ethyl, butyl, octyl, and cetyl sulphides were taken. These were prepared—by suitable dilution—in the form of very dilute standard solutions in acetic acid. The effect of varying quantities of these inhibitants on the activity of 0·05 g. of Platinum A is summarised in Fig. 1, in which, for purposes of comparison, has also been included the early part of the poisoning graph for hydrogen sulphide previously determined for the same preparation of platinum.

The quantity of poison present has been expressed, as before, in g.-mols. of the sulphide, equivalent to g.-atoms of sulphur. In view of the exceedingly small quantities (0·0025—0·05 mg.) of poison involved, confirmatory determinations, requiring the independent weighing out and dilution of a fresh small quantity of the inhibitant, were also made. These agreed well with the main determinations, as will be seen from the diagram, on which check measurements are indicated. As before, care was taken to limit the concentration of poison employed to that which was completely adsorbed by the platinum. The method of verifying the completeness of the adsorption, by testing the supernatant liquid, after allowing the platinum to settle, for freedom from poison by means of independent hydrogenation measurements has been referred to in the previous paper. The values of α, calculated from the slope of these graphs by means of the expression already given, are collected below.

Inhibitant.	$\alpha \times 10^{-5}$.	Relative toxicity.	Inhibitant.	$\alpha \times 10^{-5}$.	Relative toxicity.
Hydrogen sulphide	3·4	1	*n*-Butyl sulphide	51·2	15·1
Methyl sulphide	24·2	7·1	*n*-Octyl sulphide	87·7	25·8
Ethyl sulphide	34·0	10·0	Cetyl sulphide	116	34·1

Relative Toxicity of the n-*Alkyl Thiols*.—The corresponding poisoning graphs for ethyl-, *n*-butyl-, *n*-octyl- and cetyl-thiols are in Fig. 2. Since 0·05 g. of Platinum B was used for this

FIG. 2.



series, in place of Platinum A, the poisoning of this second preparation of platinum by methyl sulphide and butyl sulphide was also measured in order to allow a comparison between the poisoning power of the sulphides and of the thiols; and these sulphide graphs with Platinum B are also included in the figure. The graph for octylthiol is probably less accurate than the rest, since there remained, when dealing with this poison, only sufficient of the standard materials for the determination of one point. The values of α, derived from these graphs, are given below.

Inhibitant.	$\alpha \times 10^{-5}$.	Inhibitant.	$\alpha \times 10^{-5}$.	Inhibitant.	$\alpha \times 10^{-5}$.
Ethylthiol	11·0	*n*-Octylthiol	28·6	Methyl sulphide	20·4
n-Butylthiol	17·0	Cetylthiol	37·0	*n*-Butyl sulphide......	42·0

It has previously been found that, although the general sensitivity of a catalyst to poisoning may vary greatly with its physical condition—for instance with its degree of subdivision—relative toxicity, *viz.*, the ratio of the toxicity of one poison to that of another, is not changed appreciably on changing from one stock of catalyst to another. This is illustrated by the approximate constancy of the ratio between the experimentally determined values of α for methyl sulphide and butyl sulphide both for Platinum A and Platinum B:

Inhibitant.	Platinum A.		Platinum B.	
	$\alpha \times 10^{-5}$.	Ratio.	$\alpha \times 10^{-5}$.	Ratio.
Methyl sulphide	24·2	2·12	20·4	2·06
Butyl sulphide	51·2		42·0	

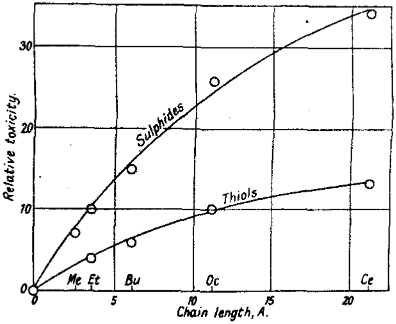
It thus becomes possible, in spite of the change in the preparation of platinum, to compare the toxicities of the thiols with those of the sulphide series generally by reducing the poisoning coefficients to a common basis. This has been done in the following table, in which *M* is the

molecular weight. In calculating the chain lengths, which are also included in the table, a value of 1·54 A. has been taken for the –C–C– link, resulting, by virtue of the alternating effect introduced into the flexed and reflexed chain by the tetrahedral valency angles, in a linear increment of about 2·52 A. in chain length for each two carbon atoms added. The chain lengths are those measured from the centre of the sulphur atom, the atomic radius of sulphur being taken as 1·04 A.

Inhibitant.	*M.*	Chain length (A.).	Relative toxicity.	Inhibitant.	*M.*	Chain length (A.).	Relative toxicity.
Hydrogen sulphide	34	—	1	Methyl sulphide......	62	2·58	7·1
				Ethyl sulphide	90	3·50	10·0
Ethylthiol	62	3·50	3·9	Butyl sulphide	146	6·08	15·1
Butylthiol	90	6·08	6·0	Octyl sulphide	258	11·12	25·8
Octylthiol	146	11·12	10·1	Cetyl sulphide	482	21·20	34·1
Cetylthiol	258	21·20	13·1				

In addition to the general increase in toxicity within each series with increasing molecular weight or chain length, it will be seen from the above table that the ratio of the toxicity of a given sulphide—which contains two hydrocarbon chains—to that of the corresponding thiol, containing

Fig. 3.



only one chain of the same length, has an approximately constant value of 2·5—2·6 : the ratios of the toxicity of ethyl, butyl, octyl, and cetyl sulphide to that of the corresponding thiol are 2·56, 2·52, 2·55, and 2·60, respectively.

Special interest is attached to the relatively great increase in toxicity brought about by the attachment to a sulphur atom of even short chains. Superimposition of a scale model of the inhibitant on a scale model of a platinum lattice—which is of the face-centred cubic type having a lattice constant of about 3·91 A., the atomic radius of platinum being about 1·38 A.—shows that there cannot at the most be more than about 9 platinum surface elements within the range of possible cover of methyl sulphide attached to the surface by its sulphur atom : yet the relative toxicity of methyl sulphide compared with that of hydrogen sulphide is, on the basis of the above experimental figures, about 7. Consequently, at least 7 potentially catalytically active surface elements must lie within the range of possible cover; in other words, at least 7 out of the 9 available elements must be catalytically active; and, since the effectiveness of the cover of surface lying within its range by a mobile chain anchored at one end is never complete, it appears probable that all the surface elements of a metal such as platinum are capable of acting catalytically. Little is known of the number of platinum surface elements covered by a molecule of adsorbed hydrogen sulphide (which, since it possesses the lowest observed toxicity, is taken as the unit in the toxicity scale) ; but, from the well-known molecular dimensions, both hydrogen sulphide and the sulphur head of a hydrocarbon chain are each of approximately sufficient size to cover one platinum surface element. If the adsorption of a sulphur head were shared by more than one platinum surface element, it would become more

difficult to account for the observed relative toxicity of short-chain compounds even on the basis of the catalytic activity of all the surface elements within range; and this difficulty would be intensified if more than one sulphur head is assumed to be adsorbed on a single platinum surface element. It accordingly appears probable that the sulphur head is adsorbed on a single surface element, and that the maximum possible area within which there is a time-probability of the occupation of surface elements by the chain is a circle of radius equal to the chain length.

With longer chains, a lesser degree of effectiveness of cover of surface lying within the range of the chain would—in view of the recession of the anchor effect—be expected than for shorter chains; and the toxicity should, as has been found, increase less rapidly than the square of the chain length: further, the effectiveness of the cover of a sulphide should, as is also the case, be greater than that of the isomeric thiol containing the same number of carbon atoms, in virtue of the presence of the sulphur anchor in the centre, in place of at the end, of the hydrocarbon chain.

The general form of the variation of toxicity with chain length is shown graphically in Fig. 3.

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212. *Chemical Constitution and the Dissociation Constants of Monocarboxylic Acids. Part VI.* (a) *The Polarity of Vinyl and Phenyl Groups.* (b) *An Apparent Linear Relationship between Dissociation Constants and Dipole Moments.*

By J. FREDERICK J. DIPPY and REGINALD H. LEWIS.

DISSOCIATION constants of further monobasic acids have been determined by the procedure already described (J., 1934, 161, 1888; 1936, 644). The following table contains the classical and the thermodynamic dissociation constants of nine acids in water at 25°, together with corresponding mobility data. In the last column all previous values in the literature are recorded; these were derived by the simple classical procedure, and confirmation was desirable to ensure complete reliance in the data, especially where differences between the strengths of acids in a series are relatively small, *e.g.*, the olefinic acids.

Acid.	Λ_0 (Na salt).	Λ_0 (acid).	$10^5K_{class.}$	$10^5K_{therm.}$	Earlier values.
p-Tolylacetic	80·0	379·6	4·35	4·27	
β-Phenylpropionic	80·4,* 80·8 *	380·2	2·23	2·19	2·27,[1] 2·2[2]
γ-Phenylbutyric	79·0	378·6	1·78	1·75	
trans-Cinnamic	80·4,* 80·6 *	380·1	3·72	3·65	3·5,[1] 3·7,[4] 3·82,[3] 3·8[5]
cis-Cinnamic (*allo*)	82·5, 82·9	382·3	$13{\cdot}5_5$	13·2	14·2,[6] 14·1[7]
Cinnamylideneacetic	78·2	377·8	3·80	3·75	
Acrylic	87·5, 87·5	387·1	5·74	5·56	5·6[1]
Vinylacetic	84·9, 84·9	384·3	4·76	4·62	3·83,[8] 4·65,[9] 4·48[10] †
Allylacetic	83·1	382·7	$2{\cdot}17_5$	$2{\cdot}11_5$	2·09,[8] 2·10[10] †

* The measurements in these cases were made on specimens of the isolated salts.

† These are thermodynamic constants, but the rest are classical values.

[1] Ostwald, *Z. physikal. Chem.*, 1889, **3**, 389. [2] Springer and Jones, *Amer. Chem. J.*, 1912, **48**, 440. [3] Schaller, *Z. physikal. Chem.*, 1898, **25**, 517. [4] White and Jones, *Amer. Chem. J.*, 1910, **44**, 188. [5] Roth and Stoermer, *Ber.*, 1913, **46**, 270. [6] Biilmann, *Ber.*, 1910, **43**, 571. [7] J. Meyer, *Z. Elektrochem.*, 1911, **17**, 982. [8] Fichter and Pfister, *Annalen*, 1904, **334**, 201. [9] Zelinsky and Isgarischew, *J. Russ. Phys. Chem. Soc.*, 1908, **40**, 1387. [10] Ives, Linstead, and Riley, J., 1933, 561.

Our thermodynamic constants for vinylacetic and allylacetic acids are in harmony with those of Ives, Linstead, and Riley (*loc. cit.*). $K_{class.}$ for *trans*-cinnamic acid approximates to that recorded by White and Jones (Ostwald's determination is appreciably lower), and $K_{class.}$ for the *cis*-acid (*allo*) is about 4% below the values of Biilmann and J. Meyer.

The mobility data are particularly interesting. The values of Λ_0 for phenylacetic and β-phenylpropionic acids appear to be identical (within the limits of experimental accuracy), but that for γ-phenylbutyric acid is distinctly less. It was to be expected that *trans*-cinnamic acid would have a mobility comparable with that for phenylpropionic acid, but the value for *cis*-cinnamic acid is 2 units higher than that of the isomeride; this may be due

to the smaller resistance offered by the more compact anion, although the diminution is comparatively large. Introduction of *p*-methyl into phenylacetic acid causes a fall of about 1 unit in mobility. With increasing anion size the Λ_0 values for the olefinic acids steadily fall. A considerable decrease is experienced in going from acrylic to vinylacetic acid, and that from the first to the third member is 4·4 units. Satisfactory mobilities for these acids could not be obtained with solutions made from the isolated salts: this procedure invariably led to values of Λ_0 several units high. It is possible that in the process of evaporation, during the preparation of the salts, sufficient alkali is present to facilitate isomeric change; although this scarcely provides an explanation of our observations, since the resultant isomeric anions here would not be expected to possess mobilities widely different from those of the original ions. The difficulty was overcome by making the stock salt solutions directly from the acids without intermediate isolation; more reasonable results were then obtained.

Experimental.

All stock solutions of acids were made up to 250 c.c., and both acid and salt solutions were prepared from water of specific conductivity 0·9—1·0 gemmho. Details of the measurements made on the acid solutions are recorded in the tables below.

p-*Tolylacetic acid.*

Cell constant.	$10^3 C$.	Λ.	$10^5 K_{class.}$	$10^5 K_{therm.}$
0·07423	1·812	55·31	4·41	4·32
	1·301	63·72	4·39	4·31
	0·9236	73·58	4·31	4·23
	0·8917	75·06	4·35	4·27
	0·5983	89·10	4·31	4·24
	0·3961	106·2	4·31	4·24

6 Determinations; limits of $10^5 K_{therm.}$: 4·23—4·32.

γ-Phenylbutyric acid.

Cell constant.	$10^3 C$.	Λ.	$10^5 K_{class.}$	$10^5 K_{therm.}$
0·1356	3·801	25·01	$1{\cdot}77_5$	$1{\cdot}73_5$
	2·525	30·47	1·77	1·74
	1·708	36·87	$1{\cdot}79_5$	1·76
0·07318	1·076	45·68	1·78	$1{\cdot}75_5$
	0·8358	51·14	$1{\cdot}76_5$	$1{\cdot}73_5$

9 Determinations; limits of $10^5 K_{therm.}$: $1{\cdot}73_5$—1·76.

cis-*Cinnamic acid.*

Cell constant.	$10^3 C$.	Λ.	$10^5 K_{class.}$	$10^5 K_{therm.}$
0·1363	2·770	76·43	$13{\cdot}8_5$	$13{\cdot}3_5$
	1·206	108·4	$13{\cdot}5_5$	13·2
	0·9028	121·5	$13{\cdot}3_5$	$13{\cdot}0_5$
0·07319	0·7017	134·9	13·5	13·2
	0·5030	153·2	13·5	$13{\cdot}2_5$
	0·4973	153·8	$13{\cdot}4_5$	13·2

17 Determinations; limits of $10^5 K_{therm.}$: $13{\cdot}0_5$—13·4.

Acrylic acid.

Cell constant.	$10^3 C$.	Λ.	$10^5 K_{class.}$	$10^5 K_{therm.}$
0·1387	12·92	25·03	5·78	5·53
	9·506	28·95	5·75	5·53
	5·776	36·73	5·75	5·55
	4·089	43·13	5·72	5·54
	1·667	65·05	5·67	5·55
	1·329	72·15	5·67	5·55

16 Determinations; limits of $10^5 K_{therm.}$: 5·53—5·61.

β-Phenylpropionic acid.

Cell constant.	$10^3 C$.	Λ.	$10^5 K_{class.}$	$10^5 K_{therm.}$
0·1363	4·201	26·97	$(2{\cdot}27_5)$	$2{\cdot}21_5$
	2·130	36·99	2·24	2·19
	1·657	41·27	2·19	2·15
0·07319	1·588	42·61	2·24	$2{\cdot}20_5$
	0·8294	57·53	2·24	2·20

15 Determinations; limits of $10^5 K_{therm.}$: 2·15—$2{\cdot}21_5$.

trans-*Cinnamic acid.*

Cell constant.	$10^3 C$.	Λ.	$10^5 K_{class.}$	$10^5 K_{therm.}$
0·1363	3·100	39·55	3·75	3·67
	1·523	54·48	3·68	3·60
	1·256	60·33	3·76	3·68
0·07319	0·9488	67·69	$3{\cdot}68_5$	3·62
	0·7958	73·43	3·68	$3{\cdot}62_5$

14 Determinations; limits of $10^5 K_{therm.}$: 3·60—3·70.

Cinnamylideneacetic acid.

Cell constant.	$10^3 C$.	Λ.	$10^5 K_{class.}$	$10^5 K_{therm.}$
0·07905	0·5254	89·59	3·87	3·81
	0·2948	113·4	$3{\cdot}79_5$	3·75
0·05421	0·1700	139·8	$(3{\cdot}69_5)$	(3·66)
	0·09232	176·5	3·78	3·75
	0·07144	192·6	$3{\cdot}78_5$	3·76

10 Determinations; limits of $10^5 K_{therm.}$: 3·75—3·81.

Vinylacetic acid.

Cell constant.	$10^3 C$.	Λ.	$10^5 K_{class.}$	$10^5 K_{therm.}$
0·1387	12·16	23·54	4·86	4·67
	6·257	32·12	4·77	4·59
	4·672	37·01	4·80	4·67
	3·463	42·13	4·68	4·57
	1·353	65·15	4·68	4·58
	1·350	65·20	4·68	4·58

13 Determinations; limits of $10^5 K_{therm.}$: 4·56—4·67.

Allylacetic acid.

Cell constant.	$10^3 C$.	Λ.	$10^5 K_{class.}$	$10^5 K_{therm.}$
0·1363	16·61	13·55	2·16	$2{\cdot}07_5$
	8·676	18·83	2·21	2·13
	6·831	21·00	$2{\cdot}17_5$	2·10
	4·883	24·56	2·14	$2{\cdot}07_5$
	4·255	26·45	$2{\cdot}18_5$	2·12
	3·364	29·73	2·20	$2{\cdot}13_5$
	2·396	34·84	$2{\cdot}18_5$	$2{\cdot}13_5$

13 Determinations; limits of $10^5 K_{therm.}$: $2{\cdot}07_5$—$2{\cdot}13_5$.

Materials.—*p*-Tolylacetic acid was prepared by the hydrolysis of *p*-toluonitrile. *p*-Methylbenzyl bromide (1·6 g.; 1 mol.) and sodium cyanide (1·5 g.; 3—4 mols.) in alcohol (20 c.c.) were heated at 100° for 30 hours. The oil remaining after evaporation and washing with water was hydrolysed by heating with 10 c.c. of dilute sulphuric acid (3 parts acid : 2 parts water) for 6 minutes, and the hot liquid filtered through glass wool; on standing, crystals of the tolyl acid separated.

Cinnamylideneacetic acid was derived from cinnamylideneacetone (Diehl and Einhorn, *Ber.*, 1885, **18**, 2321) by the haloform reaction. The ketone was shaken at 100° with an excess of fresh bleaching powder and saturated sodium carbonate solution. When evolution of chloroform had ceased, concentrated hydrochloric acid was added, and the deposit of cinnamylideneacetic acid filtered off (25% yield).

β-Phenylpropionic and *trans*-cinnamic acids were supplied by British Drug Houses, Ltd., *cis*-cinnamic and acrylic acids by L. Light and Co., and vinylacetic and allylacetic acids by Schering-Kahlbaum. γ-Phenylbutyric acid was kindly provided by Dr. E. L. Martin, to whom we are grateful.

All specimens of acids were rigorously purified. The solids (except *cis*-cinnamic acid) were finally purified by successive recrystallisation from conductivity water. The *cis*-cinnamic acid was of the *allo*-modification; it was supplied in very pure condition, and precautions were taken not to isomerise it. The liquids were redistilled until satisfactory fractions were obtained. Equivalents were determined throughout. The corrected physical constants are tabulated below, together with the best values in the literature.

Acid.	M. p. (or b. p.).	M. p. (or b. p.) from literature.
p-Tolylacetic	94°	94° (Strassmann, *Ber.*, 1889, **22**, 1230).
β-Phenylpropionic	50	48·5—49·5 (Thomas and Sudborough, J., 1912, **101**, 323).
γ-Phenylbutyric	50·5	51 (Fischer and Schmitz, *Ber.*, 1906, **39**, 2212).
trans-Cinnamic	136·5	136·8 (Kendall, *J. Amer. Chem. Soc.*, 1914, **36**, 1726).
cis-Cinnamic	68	68 (Liebermann, *Ber.*, 1890, **23**, 2510).
Cinnamylideneacetic	166	166 (Hinrichsen and Triepel, *Annalen*, 1904, **336**, 197).
Acrylic	b. p. 140·5—141/755 mm.	b. p. 140·8—141/atm. press. (Biilmann, *J. pr. Chem.*, 1900, **61**, 494).
Vinylacetic	b. p. 70·5—71/12—13 mm.	b. p. 71/12—14 mm. (Fichter and Sonneborn, *Ber.*, 1902, **35**, 938).
Allylacetic	b. p. 82—83/9·5 mm.	b. p. 90—92/16—17 mm. (Wohlgemuth, *Ann. Chim.*, 1914, **2**, 322).

Discussion.

(*a*) *The Polarity of Vinyl and Phenyl Groups.*—The effect of the vinyl group on the strengths of aliphatic acids has led inevitably to the conclusion that this group possesses an intrinsic attraction for electrons (Flürscheim, *J. pr. Chem.*, 1902, **66**, 321; J., 1909, **95**, 718; Ashworth and Burkhardt, J., 1928, 1791; Lowry, *Trans. Faraday Soc.*, 1923, **19**, 496; Henrich, "Theories of Organic Chemistry," English transl., p. 145; Ingold, *Chem. Reviews*, 1934, **15**, 239). It is also accepted that phenyl possesses a similar polar character (Ashworth and Burkhardt, *loc. cit.*; Nathan and Watson, J., 1933, 219; Ingold, *loc. cit.*), and accurate measurements of dissociation constants of acids ($10^5 K_{therm.}$ *: acetic, 1·76; phenylacetic, 4·88; diphenylacetic, 11·5) have provided sound confirmation for this (Dippy and Williams, J., 1934, 161, 1888; Jeffery and Vogel, J., 1934, 166) (compare depression in the strengths of bases measured by Carothers, Bickford, and Hurwitz, *J. Amer. Chem. Soc.*, 1927, **49**, 2908).† In addition, the vinyl and the phenyl group, when present in a conjugate system undergoing reaction, are concerned in electromeric displacements; on demand of the reagent, movement of electrons takes place in either direction.

The permanent polarisation associated with the phenyl and the vinyl group is shown in dipole moment measurements. The well-known difference between the moments of

* Distinction should be made between values of $K_{therm.}$ and $K_{class.}$. Many of the latter are acceptable in discussion (chiefly as confirmatory evidence), but comparisons should be consistent. To give clarity, values of $K_{class.}$ have been italicised; all constants are $10^5 K$.

† It is hardly possible to ascribe to phenyl a + *I* effect as suggested by Waters (*Chem. Reviews*, 1930, **7**, 415).

aliphatic and aromatic compounds (Sutton, *Proc. Roy. Soc.*, 1931, *A*, **133**, 668; cf. Bennett and Glasstone, *ibid.*, 1934, *A*, **145**, 71) demonstrates that the benzene nucleus makes some contribution to the measured moment, whilst the following data (in D) due to Höjendahl (taken from *Trans. Faraday Soc.*, Sept. 1934, Appendix) point to a similar permanent effect in the case of vinyl :—

Vinyl bromide	1·48	Allyl bromide	1·93	Allyl chloride	1·97
Ethyl bromide	2·09	*n*-Propyl bromide	2·15	*n*-Propyl chloride	2·11

Although the origin of this polarisation effect exhibited by both groups has still to be understood, it probably arises from their unsaturated character. In this connexion it is noteworthy that the introduction of a triple bond enhances the strength of an acid much more than does a double bond (phenylpropiolic acid, *590*; Ostwald, *loc. cit.*); moreover, Wilson and Wenzke (*J. Amer. Chem. Soc.*, 1935, **57**, 1265) have recently drawn attention to the marked influence of the triple bond on dipole moments.

The dissociation constants of unsaturated and phenyl-substituted acids may be interpreted on the basis of this combination of polarisation and polarisability effects.

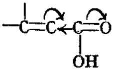
Fichter and his co-workers (*Annalen*, 1904, **334**, 201; *Ber.*, 1909, **42**, 4703) assigned classical constants to series of isomeric unsaturated aliphatic acids, noting that the order was $\beta\gamma > \alpha\beta > \gamma\delta$, and Ives, Linstead, and Riley (J., 1933, 561) confirmed these observations: *e.g.*, *n*-hexenoic acids—$\alpha\beta$, 1·98; $\beta\gamma$, 3·05; $\gamma\delta$, 1·91. The following evidence has a similar significance :

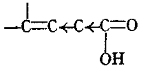
*cyclo*Hexanecarboxylic acid, *1·34*;[1] Δ^1- and Δ^2-tetrahydrobenzoic acids, *2·14* and *3·05* respectively.[2]

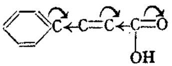
*cyclo*Heptanecarboxylic acid, *1·22*;[1] Δ^1- and Δ^2-*cyclo*heptenecarboxylic acids, *0·992* and *2·61*.[3]

[1] Zelinsky and Isgarischew, *J. Russ. Phys. Chem. Soc.*, 1908, **40**, 1379. [2] Collan, *Annalen*, 1892, **271**, 237, 271. [3] Roth, *Ber.*, 1900, **33**, 2033.

The influence of the vinyl group is observed most favourably, however, where terminal alkyl groups do not interfere, *viz.*, in acrylic, vinylacetic, and allylacetic acids. Comparable data for these acids are therefore desirable; Ives, Linstead, and Riley did not redetermine the dissociation constant of acrylic acid, while earlier values for vinylacetic acid differed greatly. The order of strengths is actually $\alpha\beta > \beta\gamma > \gamma\delta$, although the difference between $\alpha\beta$ and $\beta\gamma$ acids is less than that between $\beta\gamma$ and $\gamma\delta$ acids. These authors (*loc. cit.*, p. 563) advance the view that the double bond polarises on demand of the attacking reagent. Since the available facts are more easily interpreted, however, by supposing that an *inherent* electrical attraction *can* be associated with the vinyl group, the explanation along these lines appears more probable. The polarisation effect alone should lead to the order $\alpha\beta \gg \beta\gamma > \gamma\delta$ (cf. chloro-aliphatic acids) but actually in the $\alpha\beta$ acid (A) a conflicting effect can operate by the tautomeric mechanism so as to reduce acid strength even to the extent of producing a different order in some instances. Where the double bond and carboxyl group are not included in a conjugate system (B) there is only one influence exerted.


(A.)


(B.)

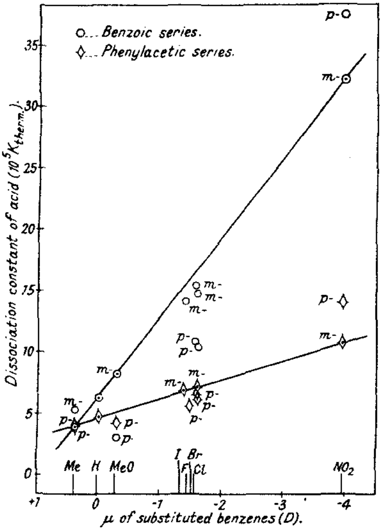

(C.)

When phenyl is attached to the terminal carbon of a fatty acid its permanent effect (called $-I$ for simplicity) alone operates, and this gradually diminishes as the chain lengthens {$Ph{\cdot}CH_2{\cdot}CO_2H$, 4·88; $Ph{\cdot}[CH_2]_2{\cdot}CO_2H$, 2·19; $Ph{\cdot}[CH_2]_3{\cdot}CO_2H$, 1·75; cf. $CH_3{\cdot}CO_2H$, 1·76; $C_2H_5{\cdot}CO_2H$, 1·336; $CH_3{\cdot}[CH_2]_2{\cdot}CO_2H$, 1·523 (the last two measurements are due to Harned, *J. Amer. Chem. Soc.*, 1933, **55**, 2379; 1934, **56**, 2039)}. This influence is also illustrated in the strengths of phenyl-substituted aliphatic primary amines (Carothers, Bickford, and Hurwitz, *ibid.*, 1927, **49**, 2908). In this system it has been shown that the

effect is still propagated from the ε-position, although it is probably correct to regard the ε-position here as comparable to the δ-position in the above acids.

Saturation of the aromatic nucleus, however, causes the strength of an acid to fall to approximately that of the fatty acids (*cyclo*hexanecarboxylic acid, *1·34*). Results comparable to this have been obtained with bases (p_{K_B}: aniline, 4·6; *cyclo*hexylamine, 10·61; methylamine, 10·64; cf. pyridine, 5·21; and piperidine, 11·13; Hall and Sprinkle, *J. Amer. Chem. Soc.*, 1932, **54**, 3482). This supports the suggestion made above, that the $-I$ effect of phenyl arises from its unsaturated nature.

It appears that abnormality occurs in the strengths of the first members of both the vinyl and the phenyl-substituted series. The difference exhibited between the strengths of phenylacetic and β-phenylpropionic acids would suggest a constant for benzoic acid far



in excess of the value actually observed (cf. strengths of aniline, benzylamine, and β-phenylethylamine; Carothers, Bickford, and Hurwitz, *loc. cit.*). The explanation is on the same lines as that provided in the case of αβ-unsaturated acids.

Phenyl, when situated conjugately in an olefinic acid, *diminishes* the strength (acrylic, 5·56; *trans*-cinnamic, 3·65); doubtless the electromeric (or mesomeric) effect of phenyl preponderates here (C).

The constant for *cis*-cinnamic acid is 4 times that of the *trans*-isomeride, and is also much in excess of that of the parent acrylic acid. Here an additional "steric" effect exists; the phenyl group is adjacent to carboxyl in the same sense as the substituent in an *o*-substituted benzoic acid, where abnormally large constants have long been observed (see Hey, J., 1928, **231**; cf. Sudborough and Lloyd, J., 1898, **73**, **93**, on esterification).

The strength of cinnamylideneacetic acid is very similar to that of *trans*-cinnamic acid, which is not surprising since opposing effects operate here owing to the additional ethylenic linkage.

In contrast to the evidence of the acids, there are instances where the polar influence of phenyl appears to be subordinate to that of methylene, the best known being in the *op*-substitution of diphenylmethane, the relative stabilities of cyanohydrins (Lapworth and Manske, J., 1930, 1976), and the nitration of guaiacol benzyl ethers (Allan, Oxford, Robinson, and Smith, *J.*, *1926*, *401*).

It is manifest, therefore, that the individual effects associated with the polarisation and polarisability of phenyl are exhibited in varying degree, according to the system in which the group is present and the nature of the reaction.

(b) *An Apparent Linear Relationship between Dissociation Constants and Dipole Moments.*—A further quantitative examination of the connexion between dipole moments and dissociation constants has been made (cf. Dippy, *Nature*, 1937, **139**, 591) since Dippy and Watson (*Chem. and Ind.*, 1935, **54**, 735) showed that the thermodynamic constants of certain substituted benzoic acids (K) and dipole moments of substituted benzenes (μ) are related by the equation $\log K = \log K_0 - C(\mu + a\mu^2)$ (see Nathan and Watson, J., 1933, 893), where K_0 is the dissociation constant of benzoic acid. If K (instead of $\log K$) is plotted against μ, a straight line can be drawn through the points involved in the earlier relationship, *viz.*, *m*-nitro-, *m*-methoxy-, unsubstituted, and *p*-methyl-benzoic acids (see fig.). It is noteworthy that *p*-toluic acid falls on the line; it appears, therefore, that the dipole moment of toluene is a measure of both the inductive effect and the permanent displacement of nuclear electrons.

The points representing *m*-nitro-, *m*-chloro-, *m*-iodo-, unsubstituted, and *p*-methylphenylacetic acids are also found to be collinear, although the slope of the line is much smaller. The divergence shown by the halogens in the benzoic series (discussed by Dippy and Watson, *loc. cit.*) has been so diminished that it is not noticeable here.

Any connexion this relationship may have with the earlier equation proposed by Nathan and Watson does not seem obvious. It may transpire that the linear equation is only an approximation to the ultimate true relationship, but nevertheless it has the undoubted advantage of being simple to apply. The conformity of the *p*-methyl substituted acids did not become clear until now.

It is interesting that the strengths of *p*-toluic and *p*-tolylacetic acids are almost identical; from the figure it is seen that the benzoic and phenylacetic straight lines intersect at a point representing these two acids. This is fortuitous, and arises, no doubt, from the fact that although phenylacetic acid is weaker than benzoic acid, yet the depressing effect of *p*-methyl in the former is appreciably less on account of the damping effect of the intervening methylene grouping.

Our thanks are due to Dr. H. B. Watson for his helpful interest in this work. We are also indebted to Imperial Chemical Industries for financial assistance and to Dr. J. W. Baker for his gift of *p*-methylbenzyl bromide.

THE TECHNICAL COLLEGE, CARDIFF. [*Received, May 7th*, 1937.]

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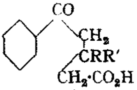
213. *The Friedel–Crafts Condensation of Substituted Glutaric Anhydrides with Benzene and the Formation of Isomeric Benzoylphenylpropionic Acids in the Reaction between Phenylsuccinic Anhydride and Benzene.*

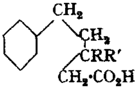
By AHMED ALI, R. D. DESAI, R. F. HUNTER, and S. M. MAKHDHUM MUHAMMAD.

ALTHOUGH the Friedel–Crafts reaction between succinic anhydrides and aromatic hydrocarbons has been extensively studied (Oppenheim, *Ber.*, 1901, **34**, 4228; Mayer and Stamm, *Ber.*, **1923**, **56**, **1424**; Krollpfeiffer and Schafer, *ibid.*, p. 620; Haworth and collaborators, J., **1932**, **1125**, **1784**, **2717**, and later), the corresponding reaction with derivatives of glutaric acid, with the exception of the condensation of glutaric anhydride itself with anisole and phenetole (Plant and Tomlinson, J., 1935, 856), has not previously been investigated.

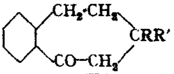
Additional interest attaches to the keto-acids (I) in that the products of their reduction by the Clemmensen method (II) would be expected to give rise to benz*cyclo*heptane derivatives (III) on cyclisation.



(I.)



(II.)

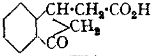


(III.)

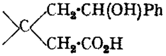
The anhydrides of glutaric acid, ββ-dimethylglutaric acid, and β-methyl-β-ethylglutaric acid reacted readily with benzene in the presence of aluminium chloride, giving the expected *γ-benzoyl-*n*-butyric acids* (I: R = R′ = H; R = R′ = Me; R = Me, R′ = Et), which yielded the corresponding *δ-phenyl-*n*-valeric acids* (II) on reduction. Attempts to convert the latter into keto*cyclo*heptane derivatives by treatment with 85% sulphuric acid were unsuccessful on account of extensive sulphonation, and we have so far been unable to devise a satisfactory method of cyclisation.

β-Phenylglutaric anhydride did not condense with benzene; internal condensation to ketohydrindene-3-acetic acid (IV) (Speight, Stevenson, and Thorpe, J., 1924, **125**, 2189) took place.

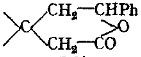
The anhydrides of *cyclo*pentane-1 : 1-diacetic acid, 3-methyl*cyclo*pentane-1 : 1-diacetic acid, and *cyclo*hexane-1 : 1-diacetic acid behaved similarly to the ββ-dialkylglutaric anhydrides, and gave rise to the corresponding keto-acids on condensation with benzene. The 1-β-*phenylethyl*-cyclo*pentane*- and -cyclo*hexane*-1-*acetic acids* (II: RR′ = C_4H_8; RR′ = C_5H_{10}) obtained by the Clemmensen method were accompanied by small amounts of neutral products, whose composition suggests that they are the *lactones* (VI) of the corresponding 1-β-hydroxy-β-phenylethyl-1-acetic acids (V).



(IV.)

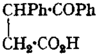


(V.)

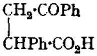


(VI.)

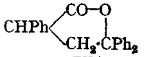
By the condensation of phenylsuccinic anhydride with benzene, Anschütz, Hahn, and Walter (*Annalen*, 1907, **354**, 150) obtained β-benzoyl-β-phenylpropionic acid (VII). We have found, however, that the isomeric β-benzoyl-α-phenylpropionic acid (VIII) and a high-melting neutral product, whose composition suggests that it is the *lactone* of γ-hydroxy-αγγ-triphenyl-*n*-butyric acid (IX) or its βγγ-triphenyl isomer (X), are also formed.



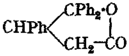
(VII.)



(VIII.)



(IX.)



(X.)

The acid (VII) proved identical with that prepared by hydrolysis of the ester obtained from the condensation of the sodio-derivative of deoxybenzoin with ethyl bromoacetate. β-Benzoyl-α-phenylpropionic acid (VIII) was also synthesised for comparison, but in poor yield, by hydrolysis of the product of condensation of ω-bromoacetophenone and phenylacetonitrile in the presence of sodium ethoxide (compare Lapworth and Hann, J., 1904, **85**, 1358).

Although indications have been previously recorded (cf. Borsche and Niemann, *Annalen*, 1933, **502**, 265) of the occurrence of isomeric products in reactions of this type, the case now described appears to be the first in which they have actually been isolated.

Experimental.

*γ-Benzoyl-*n*-butyric Acid.*—Aluminium chloride (16 g.) was gradually added to a cooled solution of glutaric anhydride (7 g., b. p. 140°/15 mm.) (Thole and Thorpe, J., 1912, **99**, 1922; Kon and Thorpe, J., 1919, **115**, 686) in benzene and after 12 hours the mixture was heated on a

water-bath until hydrogen chloride was no longer evolved. Benzene was removed by distillation, the product treated with dilute hydrochloric acid and cooled, and the final traces of benzene distilled in steam. The *keto-acid* was extracted with 10% sodium carbonate solution, precipitated by acidification, and recrystallised from hexane, forming needles (8·5 g.), m. p. 132° (Found: C, 68·5; H, 6·4; equiv., 191. $C_{11}H_{12}O_3$ requires C, 68·8; H, 6·2%; equiv., 192). The *semicarbazone*, prepared in hot alcoholic solution, crystallised in long needles, m. p. 213° (decomp.) (Found: C, 57·7; H, 6·2. $C_{12}H_{15}O_3N_3$ requires C, 57·8; H, 6·0%).

Reduction.—A mixture of γ-benzoyl-*n*-butyric acid (8 g.), zinc amalgam (12 g.), and concentrated hydrochloric acid (50 c.c.) was heated under reflux for 15 hours. The reduced acid was extracted in ether, transferred to sodium carbonate solution, precipitated by acidification, and again extracted in ether; after being dried and recovered, it solidified and recrystallisation from hexane gave δ-phenyl-*n*-valeric acid in rhombic crystals, m. p. 59° (Found for the silver salt: Ag, 38·1. Calc. for $C_{11}H_{13}O_2Ag$: Ag, 37·9%) (Baeyer and Jackson, *Ber.*, 1880, **13**, 122).

*γ-Benzoyl-ββ-dimethyl-*n*-butyric acid*, prepared from the anhydride of ββ-dimethylglutaric acid (7 g.), benzene (15 c.c.), and aluminium chloride (14 g.), formed a heavy oil. It was extracted with ether, dried, and distilled under reduced pressure, b. p. 115°/35 mm. (Found: C, 70·7; H, 7·4; equiv., 218. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%; equiv., 220). Yield, 10 g. The *semicarbazone* crystallised slowly from alcohol in plates, m. p. 178° (decomp.) (Found: C, 60·9; H, 6·9. $C_{14}H_{19}O_3N_3$ requires C, 60·7; H, 6·9%).

*δ-Phenyl-ββ-dimethyl-*n*-valeric acid*, obtained by the Clemmensen method, formed a heavy oil, b. p. 120—121°/15 mm. (Found: C, 75·4; H, 8·8. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·7%).

*γ-Benzoyl-β-methyl-β-ethyl-*n*-butyric acid* crystallised from petroleum in plates, m. p. 49° (Found: C, 71·6; H, 7·8; equiv., 235. $C_{14}H_{18}O_3$ requires C, 71·8; H, 7·7%; equiv., 235). The *semicarbazone* slowly separated from dilute alcohol in small needles, m. p. 164—165° (Found: C, 61·8; H, 7·2. $C_{15}H_{21}O_3N_3$ requires C, 61·9; H, 7·2%).

*δ-Phenyl-β-methyl-β-ethyl-*n*-valeric acid* distilled as a heavy oil at 138°/20 mm. (Found: C, 76·2; H, 9·0. $C_{14}H_{20}O_2$ requires C, 76·4; H, 9·1%).

The Reaction with β-Phenylglutaric Anhydride.—The product obtained from aluminium chloride (25 g.), β-phenylglutaric anhydride (20 g.), and benzene (20 c.c.) was freed from gummy impurities by trituration with benzene and extracted with aqueous sodium carbonate, and the crude solid obtained on acidification (m. p. 140—157°) was crystallised from alcohol. A sparingly soluble *substance* first separated in granules, m. p. 255—258°, which rose to 262° on recrystallisation (Found: C, 77·8; H, 5·5%). The more soluble portion consisted of 1-keto-hydrindene-3-acetic acid, which crystallised in thick rhombic plates, m. p. 155° (Found: equiv., 192. Calc.: equiv., 191). The semicarbazone crystallised from alcohol in needles, m. p. 260° (decomp.) (Speight, Stevenson, and Thorpe recorded m. p. 249°).

Benzylideneacetophenone (30 g.) was gradually added with shaking to a cooled suspension of ethyl sodiomalonate (prepared from 24 g. of ethyl malonate, 45 c.c. of absolute alcohol, and 3·5 g. of sodium), and the mixture was kept overnight, heated on a water-bath under reflux for 6 hours, poured into water, and acidified. An alcoholic solution of the viscous product deposited a neutral *substance* (5 g.) in hair-like needles, m. p. 255° after recrystallisation from glacial acetic acid (Found: C, 83·3; H, 5·9%). The brown oil obtained by evaporation of alcohol from the mother-liquor was heated with concentrated hydrochloric acid (50 c.c.) for 5 hours; γ-benzoyl-β-phenyl-*n*-butyric acid separated on cooling. The combined yield of this with that extracted by ether was 20 g. On recrystallisation from benzene it formed needles, m. p. 160°, and gave a semicarbazone, m. p. 220° (decomp.) (Qudrat-i-Khuda, *J. Indian Chem. Soc.*, 1931, **8**, 218).

*1-Phenacyl*cyclo*pentane-1-acetic acid*, obtained from *cyclo*pentane-1 : 1-diacetic anhydride (9 g.) (Kon and Thorpe, *loc. cit.*), separated from hexane in plates (8 g.), m. p. 85° (Found: C, 73·4; H, 7·4. $C_{15}H_{18}O_3$ requires C, 73·2; H, 7·3%). The *semicarbazone* crystallised from dilute alcohol in needles, m. p. 196° (decomp.) (Found: C, 63·2; H, 7·0. $C_{16}H_{21}O_3N_3$ requires C, 63·3; H, 7·0%).

*1-β-Phenylethyl*cyclo*pentane-1-acetic acid*, obtained on reduction of the keto-acid by the Clemmensen method, was a thick heavy oil (Found: C, 77·7; H, 8·7. $C_{15}H_{20}O_2$ requires C, 77·6; H, 8·7%). It was accompanied by a neutral substance, which appears to be the *lactone* of 1-β-hydroxy-β-phenylethyl*cyclo*pentane-1-acetic acid; on recrystallisation from benzene, it formed thick plates, m. p. 216° (Found: C, 78·75; H, 7·6. $C_{15}H_{18}O_2$ requires C, 78·3; H, 7·9%).

*1-Phenacyl-3-methyl*cyclo*pentane-1-acetic acid* crystallised from petroleum in small plates, m. p. 65° (Found: C, 73·7; H, 7·8; equiv., 262. $C_{16}H_{20}O_3$ requires C, 73·8; H, 7·7%; equiv., 260). The *semicarbazone* separated from dilute alcohol in light fibrous needles, m. p. 187° (decomp.) (Found: C, 64·5; H, 7·3. $C_{17}H_{23}O_3N_3$ requires C, 64·4; H, 7·2%).

1-*Phenacyl*cyclo*hexane*-1-*acetic acid* separated from hexane in needles, m. p. 99° (Found: C, 73·6; H, 7·6; equiv., 262. $C_{16}H_{20}O_3$ requires C, 73·8; H, 7·7%; equiv., 260). The *semicarbazone* slowly crystallised from alcohol in plates, m. p. 189° (decomp.) (Found: C, 63·7; H, 7·5. $C_{17}H_{23}O_3N_3$ requires C, 64·4; H, 7·2%).

1-β-*Phenylethyl*cyclo*hexane*-1-*acetic acid*, obtained by the Clemmensen reduction of the keto-acid, was a heavy oil (Found: C, 77·8; H, 9·0. $C_{16}H_{22}O_2$ requires C, 78·0; H, 8·9%). The neutral product which accompanied this and appears to be the *lactone* of 1-β-hydroxy-β-phenylethyl*cyclo*hexane-1-acetic acid, crystallised from benzene in thick plates, m. p. 265° (Found: C, 78·9; H, 7·8. $C_{16}H_{20}O_2$ requires C, 79·3; H, 8·2%).

The Condensation of Phenylsuccinic Anhydride with Benzene.—The product obtained from phenylsuccinic anhydride (20 g.), dry benzene (15 c.c.), and anhydrous aluminium chloride (30 g.), was extracted with aqueous sodium carbonate. The neutral residue (2—2·5 g.), whose composition suggests that it is the lactone of a hydroxytriphenylbutyric acid, had m. p. 285° (decomp.) (Found: C, 83·8; H, 5·8. $C_{22}H_{18}O_2$ requires C, 84·1; H, 5·7%). The bulk of the crude acid (m. p. 102—110°), obtained from the aqueous sodium carbonate extract, dissolved in benzene, leaving a residue (3 g.) of β-benzoyl-β-phenylpropionic acid, which on recrystallisation from dilute alcohol formed cubic crystals, m. p. 168° (Found: C, 75·7; H, 5·5; equiv., 254. Calc. for $C_{16}H_{14}O_3$: C, 75·6; H, 5·5%; equiv., 254). The βγ-diphenylbutyric acid obtained on reduction by the Clemmensen method crystallised from alcohol in prisms, m. p. 95—96° (Ruhemann, J., 1910, **97**, 459; Spring, J., 1934, 1332).

Fractional crystallisation of the benzene extract gave two fractions, m. p. 145—152° and 135—140°, and the mother-liquor slowly deposited small plates, m. p. 134°, which on recrystallisation from dilute alcohol gave α-benzoyl-α-phenylpropionic acid in needles, m. p. 154° (Found: C, 75·3; H, 5·6%; equiv., 256). On reduction this gave *αγ-diphenyl*-n-*butyric acid*, which crystallised from hexane in plates, m. p. 110° (Found: C, 79·8; H, 6·6. $C_{16}H_{16}O_2$ requires C, 80·0; H, 6·7%). The first two fractions consisted mainly of β-benzoyl-β-phenylpropionic acid, which was separated by extraction with benzene. The benzene extract furnished a further quantity of β-benzoyl-α-phenylpropionic acid. The isomeric acids were isolated in approximately equal proportion.

Synthesis of β-Benzoyl-β-phenylpropionic Acid and of β-Benzoyl-α-phenylpropionic Acid.—(A) Deoxybenzoin (5 g.) was gradually added to a solution of sodium ethoxide (prepared from 0·5 g. of sodium and 15 c.c. of absolute alcohol), and the mixture was treated with ethyl bromoacetate (4·2 g.) and heated on a water-bath under reflux for 5 hours. The viscous oil obtained by removal of alcohol and treatment with water was hydrolysed with alcoholic sodium hydroxide, and the acid was liberated by hydrochloric acid. On recrystallisation from dilute alcohol it formed thick cubes, m. p. 168° alone and when mixed with β-benzoyl-β-phenylpropionic acid obtained in the Friedel–Crafts reaction.

(B) 6 G. of phenylacetonitrile (b. p. 135—140°/35 mm.) were added to sodium ethoxide (1·2 g. of sodium, 15 c.c. of absolute alcohol), and the mixture gradually treated with ω-bromoacetophenone (10 g.). A solution of the product in alcohol was treated with potassium hydroxide (10 g., dissolved in the minimum quantity of water), and the mixture heated on the water-bath under reflux for 10 hours; ammonia was then no longer evolved. The acid obtained by purification through extraction with aqueous sodium carbonate and recrystallisation from alcohol had m. p. 154°, alone and when mixed with the specimen of β-benzoyl-α-phenylpropionic acid already described.

The condensation of glutaric anhydrides with other aromatic and hydroaromatic hydrocarbons is being investigated.

THE MUSLIM UNIVERSITY, ALIGARH, INDIA. [*Received, April 13th*, 1937.]

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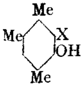
214. *The Rearrangement of* ortho-*Hydroxy-sulphones. Part VI.*

By COLIN S. MCCLEMENT and SAMUEL SMILES.

DURING a study of the sulphide (J., 1936, 327) derived from 2-nitrophenylchlorothiol and 2-chloro-*m*-5-xylenol it was observed that the corresponding sulphone (IV, X = $SO_2{\cdot}C_6H_4{\cdot}NO_2$) was very readily converted by alkali into the sulphinic acid (IX). Since in previous experiments the presence of chlorine in this position in similar 2-hydroxy-sulphones

had been found (J., 1934, 422) strongly to retard their rearrangement, it was concluded that this activity might be due to the presence of the 6-methyl group. Further investigation has confirmed this conclusion.

The material examined comprised the sulphones (I) to (VIII) [X = $SO_2\cdot C_6H_4\cdot NO_2(o)$] which were obtained by oxidation of sulphides (X = $S\cdot C_6H_4\cdot NO_2$) generated in most cases by the interaction of 2-nitrophenylchlorothiol and the relevant phenols or chlorophenols. In the case of the sulphide (VII) very poor yields of an impure product were obtained by this method and it was found expedient to chlorinate the product (VII, H instead of Cl) formed from the chlorothiol and *p*-cresol. The structures of the sulphones indicated follow from their mode of formation and from their rearrangement by alkali hydroxide, which demonstrates the ortho-situation of hydroxyl and sulphonyl. Further comment is necessary on the sulphide related to VIII (X = $S\cdot C_6H_4\cdot NO_2$). Since 3-chloro-*o*-4-xylenol was not available in sufficient quantity for the direct synthesis of the substance, the product from the chlorothiol and *o*-4-xylenol was chlorinated. The given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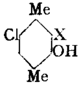
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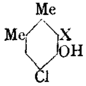
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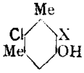
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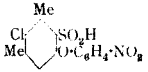
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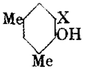
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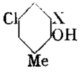
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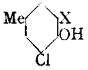
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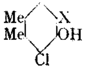
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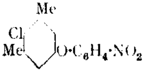

(X.)

structure is assigned to the chloro-sulphide, since (a) it is different from the sulphide (III) furnished by the interaction of the chlorothiol and 5-chloro-*o*-4-xylenol and (b) the corresponding sulphone undergoes rearrangement and therefore contains hydroxyl ortho to sulphonyl. *The rearrangement of these sulphones (I—VIII) by alkali hydroxide has been* demonstrated by the isolation of the sulphinic acids (*e.g.*, IX), which in some cases were characterised as methyl sulphones or disulphides and in all cases were desulphinated. The ethers (*e.g.*, X) then formed were isolated and identified by comparison with materials synthesised from 2-chloronitrobenzene and the relevant phenols. The formation of thioxin dioxides by elimination of sodium nitrite was not observed with the sulphones which underwent rapid rearrangement.

The relative activities of these sulphones were measured under the same conditions as those previously adopted (J., 1934, 423); since the colorimetric process then used was not easily applicable to the more active sulphones, the rearrangement was quantitatively followed in each case by titration of the excess of alkali hydroxide at intervals. For the present purpose it is unnecessary completely to reproduce the data obtained showing the course of rearrangement of each sulphone; *the following table shows the approximate time* in minutes required for the completion of the process at 50° under the adopted (*loc. cit.*) conditions of molecular dilution and concentration of akali hydroxide.

Derivatives of 2′-Nitro-2-hydroxydiphenylsulphone.

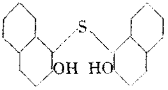
No.	Substituents.	Time.	No.	Substituents.	Time.
1	3 : 5 : 6-Trimethyl	<3	6	3 : 5-Dimethyl	95 (93)
2	5-Chloro-3 : 6-dimethyl	15	7	5-Chloro-3-methyl	>150
3	3-Chloro-5 : 6-dimethyl	12	8	3-Chloro-5-methyl	>150
4	5-Chloro-4 : 6-dimethyl	5	9	3-Chloro-4 : 5-dimethyl	>150
5	5 : 6-Benzo	(5)			

The data in parentheses are those formerly obtained by the colorimetric method. Comparison of Nos. 1, 2, and 3 with 6, 7, and 8 respectively and of 9 with the isomeride 3 clearly shows the remarkable influence of the 6-methyl group; the activity of sulphones containing this substituent is of the same order as that of the 2-naphthol derivative (No. 5).

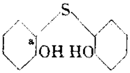
3 U

From previous studies of this intramolecular displacement there is no doubt that the activity of phenolic hydroxyl in these displacements is diminished by electron recession due to the positive *o*-sulphonyl. In seeking an explanation of the present data it is assumed that there are (Bradfield, Jones, and Spencer, J., 1931, 2907) two simultaneous *o*-positions with respect to sulphonyl and it is suggested that the 6-methyl group, by causing electron accession at the sulphonated carbon atom, at least partly overcomes the adverse influence which the sulphonyl exerts on hydroxyl and thus renders the latter more active. This view accords with the behaviour of No. 5, in which electron accession at the α-carbon atom may be inferred from the ability of 2-naphthol to assume the ketonic condition.

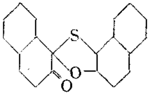
Further evidence showing the influence of 6-methyl substitution on the 2-hydroxyl group has been obtained from a study of di-*o*-hydroxysulphides such as (XI) and (XII). In (XII) the positive sulphonyl of the sulphones is replaced by the thio-group, hence substitution by 6-methyl or by the 5 : 6-benzo-group would by electron accession endow the carbon atom with increased negative character and, according to the views expressed, if this were sufficiently enhanced, the ketonic phase of the phenol might be realised. The smooth conversion of (XI) and its derivatives into the dehydro-compounds (XIII) by alka-



(XI.)



(XII.)



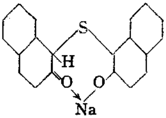
(XIII.)

line oxidation shows that this condition is attained by 5 : 6-benzo-substitution. The formation of dehydro-compounds from derivatives of (XII) has been studied by Lesser and Gad (*Ber.*, 1923, **56**, 974). These investigators held erroneous views of the structure of the products concerned, but their results are valuable, since they formulated empirical rules concerning the substitution in (XII) necessary for the formation of a dehydro-derivative. Lesser and Gad concluded that the presence of a tertiary carbon atom in the second *o*-position with respect to sulphur is an essential feature of those sulphides which yield dehydro-derivatives; sulphides without this substituent did not yield them. The experimental results have been repeated, confirmed, and somewhat extended. Inspection of the material examined by Lesser and Gad and by ourselves shows that all those sulphides which furnish dehydro-compounds are either derivatives of 2-naphthol 1-sulphide or, if derived from 2 : 2′-dihydroxydiphenyl sulphide (XII), contain the 6-methyl group. Those of the latter type which do not contain 6-methyl do not yield the simple dehydro-compounds. Altogether nine sulphides have been examined: those in group (1) gave dehydro-derivatives, those in group (2) did not.

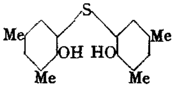
(1) 2-Naphthol 1-sulphide and its derivatives and the sulphides derived from the nuclei of (I), (II), and (IV) (X = ·S).

(2) 4-Chloro-1-naphthol 2-sulphide, the sulphide derived from (V), *p*-cresol sulphide, *p*-chlorophenol sulphide, 5-chloro-*o*-cresol 3-sulphide, 6-chloro-*m*-cresol 4-sulphide.

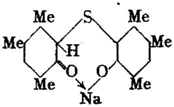
From these results the influence of the 6-methyl group on the character of di-*o*-hydroxy-



(XIV.)



(XV.)



(XVI.)

sulphides is clear. Further evidence of this influence has been obtained from the behaviour of these sulphides in presence of aqueous sodium hydroxide. It has been shown (this vol., p. 727) that even in presence of excess of this reagent 2-naphthol 1-sulphide yields an insoluble monosodium derivative to which the chelate structure (XIV) has been assigned. This characteristic behaviour is found also among derivatives of (XII) and it permits a sharp

division of these into two groups. Those which, under conditions described in the experimental part, do not yield sodium derivatives of this type are devoid of the 6-methyl group, whereas all those found to exhibit this property contain the 6-methyl substituent. For example, *m*-4-xylenol sulphide (XV), readily soluble in aqueous sodium hydroxide, is typical of the former class; *ψ*-cumenol sulphide, derived from (XV) by 6-methyl substitution, yields the insoluble covalent monosodium derivative and is typical of the latter.

The following sulphides in group (1) yielded covalent monosodium derivatives; those in group (2) did not.

(1) 2-Naphthol 1-sulphide and its derivatives, the sulphides derived from the nuclei of (I), (II), and (IV).

(2) (XV), *p*-cresol sulphide, *p*-chlorophenol sulphide, and the sulphide derived from the nucleus of (VI).

All di-*o*-hydroxy-sulphides hitherto examined which yield covalent monoalkali derivatives also yielded dehydro-compounds, whereas those incapable of giving these covalent alkali derivatives do not yield dehydro-compounds. In fact the formation of both these classes of derivative evidently depends on the ability of the hydroxy-sulphide to assume the hydroxy-ketonic structure. A similar relation exists among the derivatives of *oo'*-dihydroxydiphenylmethane; these are at present under examination.

Experimental.

The chlorocresols and chloroxylenols required for the synthesis of the 2'-nitro-2-hydroxy-sulphides were obtained by the interaction of the cresol or xylenol and sulphuryl chloride in chloroform. 2-Chloro-*m*-5-xylenol and 5-chloro-*p*-2-xylenol were prepared by the method of Lesser and Gad (*loc. cit.*), and 5-chloro-*o*-cresol and 3-chloro-*p*-cresol by the process recorded by Peratoner (*Gazzetta*, 1898, **28**, 211). In preparing the last-named it was found an advantage to remove any remaining *p*-cresol by sulphonation according to the method of Zincke (*Annalen*, 1903, **328**, 277). The yields of 5-chloro-*o*-4-xylenol obtained by the usual procedure were small and the following conditions were found more satisfactory. A solution of sulphuryl chloride (22·5 g.) in chloroform was gradually added to a cooled (15°) and shaken solution of *o*-4-xylenol (20 g.) in the same solvent. The reaction was completed by warming (30—40°), then dry air was led through the cooled mixture before the solvent was evaporated. When the residue was treated with steam, the desired material volatilised (7 g.). After purification it had m. p. 71° and was identical with an authentic specimen (Hinkel, Collins, and Ayling, J., 1923, **123**, 2973).

Sulphides derived from 2'-Nitro-2-hydroxydiphenyl Sulphide.—These were in most cases prepared by heating molecular proportions of 2-nitrophenylchlorothiol and the relevant phenol at 100—130° until hydrogen chloride ceased to be liberated. The cooled mass was triturated with ether and, if tarry matter was present, the residue was treated with charcoal in acetic acid. When the product was contaminated with bis-2-nitrophenyl disulphide, it was treated with warm 2*N*-sodium hydroxide, in which the latter is insoluble.

The sulphides of this type derived from (I), (IV), and (V) have been previously described (J., 1934, **425**, 428; 1936, **328**).

5-Chloro-2'-nitro-2-hydroxy-3 : 6-dimethyldiphenyl sulphide (II) formed yellow prisms from acetic acid, m. p. 191° (Found: C, 54·3; H, 4·2; N, 4·4; S, 10·3. $C_{14}H_{12}O_3NClS$ requires C, 54·3; H, 3·9; N, 4·5; S, 10·3%).

5-Chloro-2'-nitro-2-hydroxy-3-methyldiphenyl sulphide (VI) formed yellow needles from acetic acid, m. p. 139° (Found: C, 53·0; H, 3·5; N, 4·7. $C_{13}H_{10}O_3NClS$ requires C, 52·8; H, 3·4; N, 4·7%).

3-Chloro-2'-nitro-2-hydroxy-5 : 6-dimethyldiphenyl sulphide (III), yellow prisms, had m. p. 189° (Found: C, 54·2; H, 4·1; N, 4·5. $C_{14}H_{12}O_3NClS$ requires C, 54·3; H, 3·9; N, 4·5%).

3-Chloro-2'-nitro-2-hydroxy-5-methyldiphenyl sulphide (VII) could not be satisfactorily obtained by the usual method. It was readily formed when a solution of sulphuryl chloride (1 mol.) in chloroform was added (18°) to a suspension (1 mol.) of 2-nitrophenyl 4-hydroxy-*m*-tolyl sulphide (J., 1931, 3264) in the same solvent. After removal of the solvent under diminished pressure, the residue was purified as usual; the sulphide had m. p. 142° and was identical with a sample obtained from 3-chloro-*p*-cresol in small yield by the general method described (Found: C, 52·7; H, 3·5; N, 4·8. $C_{13}H_{10}O_3NClS$ requires C, 52·8; H, 3·4; N, 4·7%).

3-Chloro-2'-nitro-2-hydroxy-4 : 5-dimethyldiphenyl sulphide (VIII). Interaction of *o*-4-xylenol and 2-nitrophenylchlorothiol at 100° readily yielded *2'-nitro-2-hydroxy-4 : 5-dimethyldiphenyl*

sulphide (VIII, H instead of Cl), which formed yellow plates, m. p. 157° (Found: C, 61·2; H, 4·9. $C_{14}H_{13}O_3NS$ requires C, 61·1; H, 4·8%). When a suspension of this sulphide (1 mol.) in chloroform was mixed with sulphuryl chloride (1 mol.), chlorination at once began (18°). After 12 hours the solvent was removed under diminished pressure and the residue was purified as usual. The *product* had m. p. 152° (Found: C, 54·5; H, 4·2; N, 4·3. $C_{14}H_{12}O_3NClS$ requires C, 54·3; H, 3·9; N, 4·5%).

Sulphones derived from 2′-Nitro-2-hydroxydiphenylsulphone.—These were obtained from the foregoing sulphides by oxidation with hydrogen peroxide in acetic acid. A typical procedure was as follows. Excess (4 mols.) of hydrogen peroxide (30%) was slowly added to a suspension of the sulphide (4 g.) in acetic acid (20—40 c.c.; 100°), the mixture being stirred at intervals. The sulphoxide which at first separated subsequently dissolved and was replaced by the sulphone, the reaction usually being complete in 2—2½ hours. The mixture was then cooled, and the product collected and purified from acetic acid. In the case of the sulphone derived from (I) a large excess of hydrogen peroxide should be avoided, otherwise poor yields result. The products formed colourless or pale yellow, crystalline materials. The following list shows the sulphones obtained, their m. p.'s and analytical data:

Sulphones derived from (I—VIII) (X = $SO_2·C_6H_4·NO_2$).

Derived from	M. p.	Found, %. C.	H.	N.	Required, %. C.	H.	N.
I	177°	56·2	4·7	—	56·1	4·7	—
II	164	48·8	3·8	—	49·1	3·5	—
III	177	48·9	3·5	4·0	49·1	3·5	4·1
IV	164	49·3	3·6	—	49·1	3·5	—
VI	159	47·9	3·3	4·3	47·6	3·1	4·2
VII	198	47·4	3·3	4·2	47·6	3·1	4·2
VIII	155	48·8	3·6	4·0	49·1	3·5	4·1

The sulphone derived from (V) has been previously described (J., 1934, 425).

The rearrangement of these sulphones was effected by 2*N*-sodium hydroxide. In the cases of the sulphones derived from (I), (II), (III), and (IV) the process proceeded (18°) rapidly, the sparingly soluble sulphinate (compare IX) separating. In these cases the sodium salt was collected and converted into characteristic derivatives; it was also submitted to desulphination. In the cases of the sulphones derived from (VI), (VII), and (VIII) the progress of rearrangement was relatively slow and was assisted by a higher temperature (50—60°), which was maintained until the red colour of the solution had faded. After neutralisation the solutions of the sodium sulphinates were submitted to degradation by the following process. An aqueous solution of mercuric chloride (1·5 mols.) was added to the boiling solution of the sulphinate, which was maintained at 100° until sulphur dioxide was no longer liberated. The insoluble mercury derivative was washed and suspended in a boiling mixture of equal parts of alcohol and concentrated hydrochloric acid (1 hour). The cooled solution was diluted and the product which separated was purified from alcohol (charcoal). The ethers (*e.g.*, X) thus obtained were identified by comparison with samples synthesised by the method of Le Fèvre, Saunders, and Turner (J., 1927, 1168) from 2-chloronitrobenzene and the relevant phenol.

The sulphone derived from (I) yielded a sulphinic acid (compare IX) which was characterised as *2′-nitro-6-methylsulphonyl-2 : 4 : 5-trimethyldiphenyl ether*, m. p. 146° (Found: N, 4·1; S, 9·5. $C_{16}H_{17}O_5NS$ requires N, 4·2; S, 9·5%), and was degraded to *2′-nitro-2 : 4 : 5-trimethyldiphenyl ether*, prisms, m.p. 80° (Found: C, 69·7; H, 6·1; N, 5·5. $C_{15}H_{15}O_3N$ requires C, 70·0; H, 5·8; N, 5·5%). This was identical with a synthetic specimen.

The sulphone derived from (II) gave a sulphinic acid which was purified from aqueous acetone. *5-Chloro-2-o-nitrophenoxy-3 : 6-dimethylbenzenesulphinic acid* formed prisms, m. p. 125° (Found: C, 48·7; H, 3·9. $C_{14}H_{12}O_5NClS$ requires C, 49·1; H, 3·5%). It yielded a *methylsulphone*, m. p. 148° (Found: S, 9·2. $C_{15}H_{14}O_5NClS$ requires S, 9·0%), and was converted by degradation into *4-chloro-2′-nitro-2 : 5-dimethyldiphenyl ether*, m. p. 70° (Found: C, 60·8; H, 4·5; N, 4·9. $C_{14}H_{12}O_3NCl$ requires C, 60·5; H, 4·3; N, 5·0%). The latter was also synthesised.

The sulphone derived from (III) was converted into a sulphinic acid which after degradation yielded *2-chloro-2′-nitro-4 : 5-dimethyldiphenyl ether*, prisms from alcohol, m. p. 71° (Found: C, 60·9; H, 4·6. $C_{14}H_{12}O_3NCl$ requires C, 60·5; H, 4·3%), and identical with the product of synthesis.

The sulphone derived from (IV) yielded a sulphinic acid which was characterised as *4-chloro-2′-nitro-6-methylsulphonyl-3 : 5-dimethyldiphenyl ether*, prisms from alcohol, m. p. 113° (Found: C, 50·5; H, 4·4; N, 4·1; S, 9·4. $C_{15}H_{14}O_5NClS$ requires C, 50·6; H, 4·0; N, 3·9; S, 9·0%).

The corresponding *disulphide* had m. p. 142° (Found: C, 54·3; H, 4·1; S, 10·4; *M*, 630. $C_{28}H_{22}O_8N_2Cl_2S_2$ requires C, 54·4; H, 3·6; S, 10·4%; *M*, 617). Degradation of the sulphinic acid yielded *4-chloro-2'-nitro-3 : 5-dimethyldiphenyl ether* (X), m. p. 64° (Found: C, 60·8; H, 4·3; N, 5·0. $C_{14}H_{12}O_3NCl$ requires C, 60·5; H, 4·3; N, 5·0%).

The products obtained by rearrangement of (V) have been previously described (J., 1934, 422).

The sulphone (VI) yielded *4-chloro-2'-nitro-2-methyldiphenyl ether*, m. p. 39° (Found: C, 59·0; H, 4·2; N, 5·2. $C_{13}H_{10}O_3NCl$ requires C, 59·2; H, 3·8; N, 5·3%), and *2-chloro-2'-nitro-4-methyldiphenyl ether*, m. p. 57° (Found: C, 59·4; H, 4·0; N, 5·5. $C_{13}H_{10}O_3NCl$ requires C, 59·2; H, 3·8; N, 5·3%), was obtained from the sulphone (VII). Both of these ethers were identical with synthetic material.

The sulphone (VIII) gave in the usual manner *2-chloro-2'-nitro-3 : 4-dimethyldiphenyl ether*, m. p. 115° (Found: C, 60·3; H, 4·4; N, 4·9. $C_{14}H_{12}O_3NCl$ requires C, 60·5; H, 4·3; N, 5·0%).

Sulphides derived from (XII).—Those derived from the nuclei of (I), (II), (IV), and (V) were obtained by the method of Lesser and Gad (*loc. cit.*). *p*-Cresol 3-sulphide was not easily obtained in a pure condition by the method of Tassinari (*Gazzetta*, 1887, **17**, 93); it was more readily prepared by reducing the corresponding sulphoxide (Gazdar and Smiles, J., 1910, **97**, 2248) with zinc wool in boiling acetic acid until the product no longer gave a blue colour in sulphuric acid. *5-Chloro-o-cresol 3-sulphide* (compare VI) was obtained from the chloro-cresol with sulphur chloride in carbon disulphide at 18—20°. It formed leaflets from aqueous acetic acid, m. p. 145° (Found: C, 53·3; H, 3·9; Cl, 22·6. $C_{14}H_{12}O_2Cl_2S$ requires C, 53·3; H, 3·8; Cl, 22·5%). 4-Chlorophenol 3-sulphide, m. p. 174°, was obtained in a similar manner.

The formation of dehydro-derivatives from sulphides of this type (compare Lesser and Gad, *loc. cit.*) was examined by treating their shaken alkaline solutions with a slight excess of aqueous potassium ferricyanide. The dehydro-derivatives, if formed, separated as orange or red amorphous solids, which were removed by solution in ether. The sulphides which did not form the simple dehydro-derivatives yielded amorphous, pale green material insoluble in ether. The isolation of the dehydro-compounds by this method is not usually easy, since the ethereal extract is apt to contain unchanged sulphide as the covalent sodium compound. They were more readily obtained in a purer condition by warming a benzene solution of the sulphide in presence of excess of lead peroxide. The solid remaining after evaporation of the solvent was purified from aqueous acetic acid; the products formed orange micro-crystalline or amorphous powders. *Dehydro-5-chloro-*p*-2-xylenol 3-sulphide* (compare II) had m. p. 165° (Found: C, 56·7; H, 4·4. $C_{16}H_{14}O_2Cl_2S$ requires C, 56·3; H, 4·1%). *Dehydro-ψ-cumenol sulphide* (compare I) had m. p. 97° (Found: C, 71·6; H, 6·6. $C_{18}H_{20}O_2S$ requires C, 72·0; H, 6·7%). Dehydro-2-chloro-*m*-5-xylenol 6-sulphide (compare IV), an amorphous orange material, was not further investigated, since Lesser and Gad (*loc. cit.*) have already examined its bromine derivative.

The formation of covalent monoalkali derivatives from these sulphides (compare this vol., p. 727) was examined by reaction with aqueous sodium hydroxide (2 mols., 5%). The covalent alkali derivatives, if formed, separated as insoluble crystalline materials, which were removed by solution in ether and isolated by drying in a current of air at 25° after the solvent had been evaporated. Sulphides of this type which did not yield the covalent derivatives completely dissolved in the alkaline medium; ether which had been shaken with these solutions contained only a small amount of the sulphide concerned and no sodium salt. The following covalent monosodium derivatives were all readily soluble in moist ether, forming yellow solutions, and moderately readily soluble in warm chloroform; partial dehydration sometimes took place in the latter solvent.

*Monosodium 5-chloro-*p*-2-xylenol 3-sulphide*, m. p. 255° after some loss of water (Found: Na, 5·1. $C_{16}H_{15}O_2Cl_2SNa,4H_2O$ requires Na, 5·1%).

Monosodium ψ-cumenol sulphide, m. p. 245° after losing some water at 100° (Found: Na, 5·9. $C_{18}H_{21}O_2SNa,4H_2O$ requires Na, 5·8%).

*Monosodium 2-chloro-*m*-5-xylenol 6-sulphide* lost water more readily than the derivatives already mentioned; dehydration was completed at 115° in a vacuum (Found: Na, 6·3; H, 4·1. $C_{16}H_{15}O_2Cl_2SNa$ requires Na, 6·3; H, 4·1%). The anhydrous material was insoluble in dry ether and did not melt, having evidently assumed the electrovalent state. In presence of moisture it reverted to the covalent state, being readily soluble in moist ether.

The authors thank Dr. L. Hinkel for an authentic specimen of 5-chloro-*o*-4-xylenol and are also indebted to the Ministry of Education for Northern Ireland for a grant which enabled one of them to take part in these experiments.

King's College, London. [*Received, April 28th*, 1937.]

215. *Combination of Fatty Acids with Nitrogen Bases. Part IV. Diethylamine and Propionic Acid: Densities, Surface Tensions, Conductivities, and Viscosities of the Liquid Anhydrous System.*

By R. N. Coleman and E. B. R. Prideaux.

The variation of certain physical properties of the systems, piperidine–lower fatty acids, has been studied in Parts I, II, and III (J., 1936, 1346; this vol., pp. 4, 462). This work has now been extended to another organic base in order to ascertain whether the results obtained with piperidine are typical of the system, moderately strong base–weak acid, or whether they are peculiar to this heterocyclic base. The base required was an aliphatic amine, which should be liquid at 25° and have a dissociation constant of not less than 10^{-4}. The only one fulfilling these conditions, besides being readily obtainable and not too volatile, is diethylamine, which has b. p. 55·5° and K_b $1{\cdot}26 \times 10^{-3}$ at 25°. The volatility is, however, rather greater than desirable, and special precautions have to be taken on this account.

Since it was not considered necessary to carry out experiments with all the acids previously studied, propionic acid was selected as being typical of the series. The surface tensions, densities, conductivities, and viscosities of the acid–base system were measured, and also the temperature coefficient of the salt in the case of the last three properties. Molar volumes, parachors, and conductivity–viscosity products were deduced from these data.

Experimental.

The diethylamine was of the best quality obtainable, practically the whole of the sample distilling at the correct b. p. The purity was checked by titration, and the liquid was then used without further purification. Specimens of the diethylamine salts of the acids, propionic to octoic, were prepared by weighing out a suitable quantity of the acid, and adding slightly less than the required volume of diethylamine from a graduated pipette. The exact amount was reached by adding the base drop by drop. These salts were colourless, deliquescent, viscous liquids, miscible in all proportions with alcohol, ether, and benzene. The propionate and butyrate mixed in all proportions with water to give clear solutions. On diluting a concentrated solution of the salts of the higher acids, at a certain point cloudiness was observed, which persisted as more water was added. Since these acids are only partly miscible with water, it seems probable that this cloudiness is due to hydrolysis of the salt, rather than to the partial miscibility of the salts themselves in water. This behaviour is also observed with the piperidine salts. The propionate and butyrate solidified to colourless needles having well-defined m. p.'s of 13° and 23° respectively. The *iso*valerate gave a less sharp m. p. of *ca.* 6°; the higher members of the series failed to crystallise. A large molecular volume thus appears to be associated with a strong tendency to supercool.

On account of the volatile nature of diethylamine, each individual mixture was prepared by first weighing out a suitable quantity of propionic acid and then adding the required volume of diethylamine, with cooling in ice. The bottle was stoppered and weighed, and the contents thoroughly mixed by vigorous shaking.

The viscosity and conductivity were first measured in a thermostat at 25° by the methods described in Part II. Drying tubes on both limbs of the viscometer contained anhydrous sodium sulphate and soda-lime. The liquid was transferred by pipette to the twin capillary-tube apparatus (Part I), and the capillary rise determined. A pyknometer was then filled, and the density of the mixture measured. Every precaution was taken throughout to ensure that the liquid was in contact with the atmosphere for a minimum of time, on account both of the volatility of the base and of the somewhat deliquescent nature of the mixtures.

The temperature coefficients of density, conductivity, and viscosity of the salt were determined exactly as before. Conductivities were steady and reproducible, and were not changed even after the sealed conductivity cell had been kept for 6 hours at 100°. Efforts to obtain the variation of surface tension with temperature failed, as it was found that, especially at higher temperatures, the difference in height of the liquid in the two capillary tubes increased with time, and that, on creating a new meniscus, a somewhat lower value was again obtained. This was probably due to evaporation of diethylamine, produced by an appreciable molecular dissociation of the salt, which would give a surface in the meniscus richer in acid, and hence with

a higher surface tension. This effect was also observed to a lesser extent with mixtures containing the base in excess. At 25°, however, the change was only 0·002 cm. in 20 minutes, so that a true value at this temperature was obtained by first allowing the liquid in the vessel to attain the temperature of the thermostat, and then immersing the capillaries and taking the reading within 15 minutes.

Properties of the system diethylamine–propionic acid.

Acid, mols. %.	d.	σ.	$\kappa \times 10^3$.	η.	n.	V.	Λ.	$\Lambda\eta \times 10^4$.
0·0	0·7045	19·28	0·000	0·0035	0·000	103·8	0·000	0
11·8	0·7520 *	—	0·012	0·010 *	—	—	0·010	1
18·6	0·7800 *	—	0·304	0·015 *	—	—	0·153	23
23·8	0·8021	21·57	0·701	0·021 *	0·312	119·9	0·270	57
32·3	0·8410	23·95	1·165	0·044	0·477	129·0	0·315	138
41·9	0·8890	29·20	1·31	0·153	0·721	142·4	0·259	396
46·8	0·9133	30·97	1·25	0·306	0·879	151·5	0·215	659
50·0	0·9260	31·45	1·21	0·461	1·000	159·0	0·192	887
52·7	0·9348	31·56	1·19	0·550	0·898	149·6	0·198	1090
55·6	0·9422 *	—	—	0·562	—	—	—	—
57·7	0·9473	31·63	1·36	0·539	0·733	134·9	0·250	1348
64·7	0·9623	31·32	1·75	0·379	0·545	118·5	0·380	1441
75·9	0·9820	30·21	2·93	0·168	0·318	99·1	0·914	1535
80·6	0·9872 *	—	3·29	0·112 *	—	—	1·270	1422
84·2	0·9902 *	—	3·10	0·080 *	—	—	1·471	1177
87·6	0·9913	28·13	2·52	0·056 *	0·142	85·1	1·512	847
92·4	0·9906 *	—	0·829	0·031 *	—	—	0·816	253
97·0	0·9880 *	—	0·009	0·017 *	—	—	0·022	4
100·0	0·9844	26·06	0·000	0·0102	0·000	75·2	0·000	0

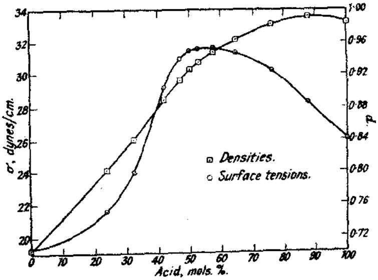
* Interpolated.

Properties of diethylammonium propionate.

Temp.	d.	$\kappa \times 10^3$.	η.	Λ.	$\Lambda\eta \times 10^4$.	Temp.	d.	$\kappa \times 10^3$.	η.	Λ.	$\Lambda\eta \times 10^4$.
20·2°	0·9296	1·02	0·587	0·161	948	44·4°	0·9118	2·16	0·196	0·349	684
25·0	0·9260	1·21	0·461	0·192	887	49·4	0·9080	2·52	0·161	0·408	658
30·0	0·9221	1·42	0·364	0·227	825	54·8	0·9042	2·83	0·133	0·461	613
34·6	0·9189	1·67	0·295	0·267	789	59·8	0·9003	3·24	0·111	0·530	588
39·4	0·9154	1·90	0·240	0·306	733						

In the tables, d is the density, σ the surface tension, κ the specific conductivity, η the viscosity, n the molar fraction of salt, V the molar volume, and Λ the molar conductivity.

FIG. 1.



DISCUSSION.

Densities.—On the basic side of the curve (Fig. 1) an almost linear graph is obtained, closely resembling that for the systems containing piperidine. The maximum is considerably displaced to the side of excess acid, *i.e.*, at 88 mols. % of acid. Piperidine–propionic acid showed this effect to a less extent, the maximum being at about 60 mols. %. There

is thus contraction when the acid and the base combine to form the salt, but the volume of a mixture of the salt with acid is considerably less than that of a mixture containing an equal excess of base, even allowing for the smaller specific volume of the acid as compared with the base. This may be perhaps explained by changes in the ionisations of the salt in the two media (see p. 1026). The variation of density of the salt with temperature is linear, and may be expressed by the equation $d = 0{\cdot}9445 - 7{\cdot}35 \times 10^{-4}t$.

Surface Tensions.—Fig. 1 indicates that the general character is similar to that of the systems piperidine–lower fatty acids: the maximum is displaced from the salt concentration towards the side of that component having the higher surface tension: in the present case it occurs with excess of acid, but in the piperidine systems, with acids of higher molecular weight than butyric, it is found on the basic side, the acids having the lower surface tension. The same three factors discussed in Part I (*loc. cit.*, p. 1350) are again operative. The predominant effect is the high surface tension of the salt, and the rounded summit is explained by its molecular dissociation, which is diminished by excess of either constituent. The small amounts of the highly capillary-active diethylamine, thus produced, lower the surface tension of the salt to a value below that shown by a mixture containing a small excess of acid. With the addition of excess of base the surface tension falls more rapidly than the mixture law allows, on account of surface adsorption of the base, until, the surface layers becoming saturated, the rate of change of surface tension is diminished, and a concave curve results.

Molecular Volumes.—The molecular volumes of mixtures of the salt with excess of acid and of base were calculated as before, and when plotted against the molar fractions of salt in the mixtures give a graph similar in all respects to those of the piperidine systems (Part I). The points lie slightly below the values required by the mixture law, the deviation being more marked on the acid side. The difference between the sum of the molecular volumes of acid and base and that of the salt is 20·0, *i.e.*, there is a contraction of 11·2% on combination. The corresponding figure for piperidinium propionate is 10·2%. This contraction, presumably due to the formation of ions, is thus of the same order in both salts.

Parachors.—The experimental value of the parachor of diethylamine is 217·5, the value calculated from Sugden's constants being 219·8. The observed parachor of the salt is 376·4, being 22·0 units below the calculated value of 398·4, a deviation of 5·5%. This is of the same order, although not quite as great, as the deviation of 26·7 (6·5%) in the case of piperidinium propionate. This parachor deviation thus seems to be characteristic of the formation of ions by the transference of the proton from the acid to the base, and to this it may be therefore largely ascribed—together with the possibility of association, and the effects of surface adsorption. It may be noted that the parachor of diethylammonium propionate, on the basis of Mumford and Phillips's constants (J., 1929, 2112), is 377, *i.e.*, practically the same as the observed value. An error was made in recording the parachors of the salts of piperidine calculated by this system (Part I, *loc. cit.*, p. 1353). The values are all 5 units low, and should read:

Salt.	P of salt.	P, obs.	Salt.	P of salt.	P, obs.
Propionate	386	382·6	Hexoate	506	491·7
Butyrate	426	418·5	Heptoate	546	527·9
*iso*Valerate	466	453·6	Octoate	586	568·2

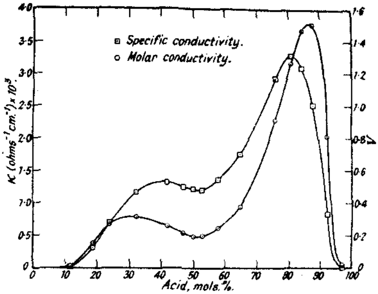
This does not affect the conclusions drawn therefrom. The characteristics of the basic side of the surface-tension curve make it apparent that the parachors of mixtures of salt and excess base will be too greatly influenced by the effects of surface adsorption to have any real significance. Moreover, Hammick and Andrew (J., 1929, 754) do not consider that the mixture law for parachors will hold when the surface tensions of the two liquids differ by more than 7 dynes/cm.

Conductivities.—The specific and molar conductivities of diethylammonium propionate are of much the same order as those of the piperidine salt. The values are rather greater, but, as will be shown, this is probably due to the lower viscosity. The temperature coefficients, $(d\kappa/dt)/\kappa$, are 0·034 at 25° and 0·026 at 60°. These are similar to the corre-

sponding values for piperidinium heptoate, *viz.*, 0·049 and 0·028, so the same conclusions may be drawn, that the diethylamine salt belongs to the class of weak electrolytes. The molar conductivity varies with temperature according to the equation $\Lambda = 9{\cdot}37 \times 10^{-5}t^2 + 1{\cdot}95 \times 10^{-3}t + 0{\cdot}084$.

Fig. 2 shows the variation of specific and molar conductivities of the system diethylamine–propionic acid. Molar conductivities are calculated by assuming that the salt alone

Fig. 2.



conducts the current, and are therefore obtained on the basis of g.-mols. of salt present per litre of the mixture. As before, two maxima are observed, with a minimum close to 50 mols.%; that on the acid side is much more pronounced than that on the basic side. The

Fig. 3.

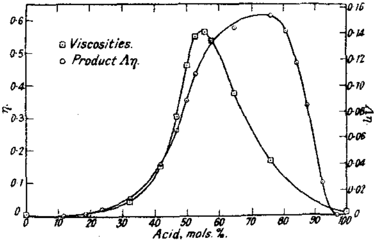
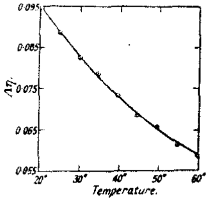


Fig. 4.



conductivity of the salt is thus considerably greater when dissolved in propionic acid than when in diethylamine.

Viscosities.—Variation of viscosity of the system is shown by Fig. 3. The maximum is again displaced towards the component having the higher viscosity, but the displacement is slightly greater than for the system piperidine–hexoic acid, *viz.*, 5 mols.% instead of 3 mols.%. The curve is also not symmetrical but falls more steeply on the basic side. The variation of viscosity with temperature is expressed by the equation $\log \eta = 787{\cdot}4/(T - 104{\cdot}1) - 4{\cdot}397$, where T is the absolute temperature, in accordance with Andrade's general formula for associated liquids (*Nature*, **1930**, **125**, **309**).

Conductivity–Viscosity Products.—Experimental viscosity values, together with values interpolated from the curve, were used to calculate the product $\Lambda\eta$, the variation of which with concentration is shown by Fig. 3. An indication of the proportion of free ions con-

tained by the salt in the various mixtures is thus obtained. There is some departure of the experimental points from a smooth curve near the maximum, but here both the Λ and the η values are rapidly changing in opposite senses, and small experimental errors will be increased in the product. The two maxima of the Λ curve are reduced to a single maximum, as was the case with the piperidine system, but whereas in that system there was a shift of this maximum only 5 mols.% away from the equivalent point to the acid side, it is now removed 25 mols.% in the same direction. The proportion of ions in the salt seems, therefore, to be definitely increased by the addition of excess of acid. This would appear to be contrary to the general non-ionising character of propionic acid as a solvent, so the effect is perhaps due to the formation of an acid salt which gives more dissociated ions than the normal salt. This explanation has already been advanced to explain the less marked displacement in the piperidine system. The presence of a relatively greater proportion of ions in excess acid than in excess base is also suggested by the form of the density curve, since low volumes (high densities) are to be associated with ionisation.

The variation of $\Lambda\eta$ of the salt with temperature (Fig. 4) shows the same characteristics as that of piperidinium heptoate; $\Lambda\eta$ is far from constant and falls rapidly with rising temperature, the rate of fall, however, decreasing at higher temperatures. The values of the molar conductivity and of $\Lambda\eta$ are here compared with those of the salts discussed in the previous papers:

	Λ.	Λη.		Λ.	Λη.
Piperidinium propionate...	0·0851	0·2374	Piperidinium heptoate	0·0627	0·0860
Piperidinium hexoate	0·0657	0·1042	Diethylammonium propionate	0·192	0·0887

Hence, although diethylammonium propionate has a higher molar conductivity than any of the other salts, yet it has a $\Lambda\eta$ value of the same order as that of the heptoate, so that, according to this, the degree of ionisation of the propionate of diethylamine is the same as that of the higher members of the series of the piperidine salts of the lower fatty acids.

UNIVERSITY COLLEGE, NOTTINGHAM. [*Received, May 7th,* 1937.]

216. *Azo-indicators with a Quaternary Ammonium Group.*

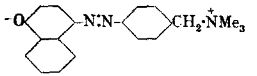
By G. SPENCER HARTLEY.

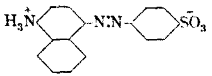
IF acidimetric indicators are to be used in aqueous solutions containing long paraffin-chain cations or positively charged colloids, it is desirable (Hartley, *Trans. Faraday Soc.*, **1934**, **30**, **444**) that their colour-ions should have a resultant positive charge in both the acid and the alkaline form. Among commercially available compounds, the choice is at present restricted to those of the di- or tri-amino-(or alkylamino-)triphenylmethane class, or compounds of the quinoline-blue (Colour Index, 1924, No. 806) type. The former cover only the very acid range and, in some cases (*e.g.*, crystal-violet), show complex fading phenomena (Adams and Rosenstein, *J. Amer. Chem. Soc.*, **1914**, **36**, **1452**), which are sufficiently rapid to make their use inconvenient. The latter are too unstable to be of utility.

During the work referred to, the author prepared some azo-indicators from a specimen of β-*p*-nitrophenylethyltrimethylammonium iodide kindly supplied by Dr. E. D. Hughes, to whom he is also indebted for valuable advice. These compounds were satisfactory, and means of preparing analogous ones from a more readily available material were, therefore, sought.

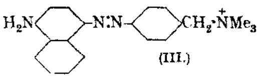
It is believed that the compounds described, which are very easily prepared, may have considerable interest apart from the particular purpose for which they were designed. Another application for one of them, in moving-boundary transport-number measurements (Samis, *Trans. Faraday Soc.*, **1937**, **33**, **469**), has already been described. In the study of hydrogen-ion-controlled reactions and equilibria (particularly biochemical), increasing attention must be paid to salt effects if satisfactory progress is to be made. These effects

are functions mainly of the valency-type of the ions concerned (Guggenheim and Schindler, *J. Amer. Chem. Soc.*, 1934, **38**, 543) and it is desirable, therefore, to extend, as do the compounds described, the range of valency-type available in indicators. Finally, these compounds, in common with other quaternary ammonium salts, have a higher solubility than most other salts of corresponding complexity. This is particularly marked in the case of one " zwitterionic " indicator prepared, the compound (I) being far more soluble in cold

(I.) 

 (II.)

alkaline water than is necessary for indicator work. Its counterpart (II), with reversed signs (we make no attempt here to represent the actual location of the labile charge),



(III.)

is so sparingly soluble that it is precipitated when a solution of the sodium salt, in concentration such as is used in indicator work, is acidified. It is for this reason that α-naphthylamineazo-compounds have been little used as indicators. The ion (III) forms very soluble salts and thus renders more available the yellow–purple colour change of the α-naphthylamineazo-group (between p_H *ca.* 3·5—5·5).

The quaternary ammonium indicators described are neither more nor less stable than other azo-indicators. They are easily decolorised by reducing agents, but are otherwise permanent, except that the naphthylamine compounds fade in a few hours at 100°.

Experimental.

p-Nitrobenzyl chloride was the starting material. From this, the *p*-aminobenzyltrimethylammonium ion was prepared, diazotised in the usual way in acid solution, and coupled with various aromatic amines. Reduction of the nitro-group could not be made the first step in the preparation, as only tarry condensation products were obtained. If, however, the chloride is first replaced by quaternary nitrogen, reduction may then be effected by any of the usual agents in acid solution. Of these, iron was found most convenient.

It was found that trimethylamine and nitrobenzyl chloride unite very readily, and special solvents, such as nitromethane, were unnecessary. The procedure adopted was to dissolve the nitrobenzyl chloride in about 3 times its weight of acetone, and then to add (as 33% aqueous solution) trimethylamine in about 50% excess of the theoretical quantity. The initially cloudy mixture became clear after a few minutes' shaking. Heat was evolved, but insufficient to necessitate external cooling. The mixture was kept until a sample remained clear when the amine and acetone were boiled off. A little water was then added to the bulk, and the amine and acetone driven off by heating, a few drops of hydrochloric acid being added when the amine odour had disappeared, to reduce possible hydrolysis of the quaternary ammonium salt. The resulting aqueous solution of *p*-nitrobenzyltrimethylammonium chloride was yellow but quite clear. The iodide could be precipitated in pale yellow plates by addition of excess of potassium iodide, but separation of this compound was not considered necessary in the main preparation.

To the solution of nitro-salt (about *M*), prepared as above, 5% of the theoretical amount of hydrochloric acid was added, and then, in small quantities and with constant stirring, iron filings. Since the reaction was very vigorous and evolved considerable heat, each addition of iron was delayed until the temperature of the reaction mixture had fallen below 70°. Cessation of rise of temperature on further addition of iron was taken to indicate the end of the reaction. A slight excess of ammonia was then added, and air blown through the mixture to oxidise ferrous to ferric hydroxide. The filtrate, diluted by washing to about *M*/3 (assuming 100% yields), was red, but gave no test for iron in any circumstances, the colour being presumably due to an organic by-product. Diazotisation of the amino-salt was carried out directly in this solution after addition of nitric acid.

Coupling with aromatic amines proceeded most quickly when the reaction mixture was nearly neutralised with ammonia. After being kept for 24 hours, the mixture was made definitely alkaline with ammonia, and extracted several times with benzene to remove free amine and any by-products not ionised in alkaline solution. In most cases, crystalline indicator nitrate was already present in the aqueous layer, but more complete precipitation was ensured by adding

a large excess of ammonium nitrate and keeping the mixture cold for 24 hours. The nitrates (less soluble than the chlorides and preferable in use to the iodides) were recrystallised several times from hot water. The yields of once-recrystallised products were 50—70% of the theoretical for the amount of nitrobenzyl chloride used.

A small amount of brown gummy material made the first filtration slow, but disappeared in recrystallisation. A cleaner first precipitate was obtained in a preparation when the amino-salt was isolated as iodide (and reconverted into nitrate by silver nitrate solution) before diazotisation. This salt is, however, extremely soluble in water, and its isolation therefore very wasteful.

Mononitrates were obtained in this way from coupling with the following amines. The appearance of the salts, colour changes of the solutions (alkaline first), and the approximate p_H values for the half-changed condition are given. The indicators cover a range of about one p_H unit on either side of this value and are usable in concentrations between 10^{-5} and $10^{-6}N$.

Amine.	Appearance.	Colour change.	p_H.
(1) Dimethylaniline	Bright orange-red plates	Orange-yellow ⟶ bright pink	3·3
(2) α-Naphthylamine	Small dark purple plates	Orange-yellow ⟶ purple-red	4·5
(3) Dimethyl-α-naphthylamine	Very fine, bright red precipitate, which could not be removed by filtration, but was centrifuged	Similar to (2)	
(4) β-Naphthylamine	Fine, bright red precipitate	Yellow ⟶ red	1·3

No salt could be isolated from the reaction mixture when *m*-phenylenediamine was used, and a sample of the mixture showed a very indefinite colour change.

The constitution of these compounds is obvious from the method of formation, the cations in the salts and in alkaline solution having formulæ similar to (III). The following confirmatory observations were made.

(*a*) No colour was extracted from alkaline solution by benzene. It would be were the *strong* basic group not present.

(*b*) After warming with alcoholic potash and dilution with water, a benzene extract had a yellow colour, the quaternary group having been hydrolysed to amine and alcohol.

(*c*) The salts were more soluble in acid than in alkaline solution, indicating further ionisation.

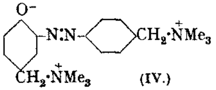
(*d*) The colour in buffer solution was not displaced by addition of a small amount of cetylpyridinium chloride (for significance, see Hartley, *loc. cit.*).

(*e*) Addition of neutral salt (*e.g.*, potassium chloride) to solutions in acetate–acetic acid buffers displaced the colour towards that of the acid form, which is, therefore, the more highly charged (cf. Guggenheim and Schindler, *loc. cit.*).

(*f*) A conductimetric titration of the dimethylaniline *compound* was made by adding successive weighed amounts of the solid to a $N/100$-nitric acid solution in a conductivity vessel (Found : equiv. as a base, 385 ± 5%. $NMe_2·C_6H_4·N{:}N·C_6H_4·CH_2·NMe_3NO_3$ requires equiv., 359).

(*g*) A sample of *iodide* was prepared from the nitrate of the dimethylaniline compound by recrystallising it twice from excess of potassium iodide solution and twice from water. An acid solution of this was titrated against silver nitrate electrometrically (Found : I, 28·9. $NMe_2·C_6H_4·N{:}N·C_6H_4·CH_2·NMe_3I$ requires I, 30·0%).

By coupling the diazotised amino-salt with diphenylamine or benzylaniline, other indicators could doubtless be made which would be useful at lower p_H values than are those described. We were guided in our choice of amines by an endeavour to make indicators which could be used in the more generally important range of $p_H > 6$. In this we were not successful, and an attempt was therefore made to prepare a compound of another type, also having, but by a different mechanism, a resultant positive charge in alkaline solution. Two equal portions of the amino-salt solution were treated with nitrite. One was then heated, to replace the amino- by a hydroxyl group, made alkaline, and cooled, and the other solution was added. A dark brown colour developed, presumably due to the ion (IV), but no anion could be found to give a precipitate with it. The behaviour of a diluted solution of the reaction mixture, however, confirmed formula (IV). Tests (*a*)—(*e*) [but with a phosphate buffer in (*d*) and (*e*)] gave the same results as before. The colour change was from darker (alkaline) to lighter (acid) yellow in the range p_H 7—8, as would be expected for a phenolic azo-compound. The colour faded completely in strong acid solution and could not be restored. In other respects the compound appeared normally stable.



(IV.)

For the purpose of comparison with other zwitterionic indicators, one was prepared from the diazotised amino-salt by coupling with α-naphthol in alkaline solution. The high solubility of

the internal salt (I) precipitated from the reaction mixture has already been mentioned. It could conveniently be recrystallised from hot water. The solution was red when alkaline and orange-yellow when acid, the half-change point being about p_H 8·5.

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217. *The Kinetics of the Decomposition of Carbonyl Selenide on an Allotropic Selenium Surface.*

By R. H. PURCELL and F. D. ZAHOORBUX.

FEW heterogeneous gas reactions are known in which the catalytic surface is continuously renewed by the deposition of one of the reaction products from the gas phase. This is unfortunate, since such a process should be a good one for maintaining a constant catalytic surface, and for showing any change of the surface with temperature or other reaction conditions. Stibine, which decomposes at room temperatures, was studied by Stock and Bodenstein (*Ber.*, 1907, **40**, 570), who found that, after a sufficiently thick initial coating of antimony had deposited on the reaction bulb, reproducible values were obtained which could be expressed by $dp/dt = kp^n$. This was shown to be due to the change with pressure p of the amount of stibine adsorbed on the surface. The splitting up of carbonyl selenide into carbon monoxide and selenium appeared to provide another example of this type of reaction. The substance was first prepared in a state of purity by Pearson and Robinson (J., 1932, 652), who described it as a colourless liquid, b. p. $-$ 22·9°/725 mm., m. p. $-$ 122·1°, readily decomposed by heat. They found that, when perfectly dry, it could be kept at room temperature for considerable periods without change. The simplicity of the reaction and the absence of side reactions suggested that the kinetics of the decomposition would be worthy of study. This has proved to be the case, for it has been found that the selenium surface on which the reaction proceeds can exhibit phase allotropy. Its catalytic activity changes with the allotropic transformations, but a means has been found of accounting for the complications thereby introduced.

EXPERIMENTAL.

(a) *Preparation and Re-determination of Vapour Pressure of Carbonyl Selenide.*—The carbonyl selenide was prepared by Pearson and Robinson's method (*loc. cit.*) by passing pure dry carbon monoxide over molten selenium at a dull red heat and condensing the product in liquid oxygen. We used silica instead of porcelain reaction tubes, and the yield was thus increased four-fold while the carbon dioxide present was much reduced. This is probably due to the well-known catalytic activity of porcelain for the reaction $2CO \longrightarrow CO_2 + C$; the porcelain might also have been slightly porous and have allowed some atmospheric oxygen to come into the reaction tube, there combining with the carbon monoxide.

The carbonyl selenide was purified after being transferred to a storage apparatus shown in Fig. 1. Small head fractions were then distilled from the liquid when near its m. p. until the vapour pressure of the residue, in a bath of solid carbon dioxide and ether, was constant. It was apparent after the first preparation that Pearson and Robinson's vapour-pressure results were considerably high, and consequently a new series of determinations was made.

A middle fraction of the already purified carbonyl selenide was transferred to a condensation tube, and the pressure of the vapour above the liquid read on a mercury manometer to 0·05 mm. with the aid of a cathetometer. Constant-temperature baths were prepared from the purest obtainable organic liquids, which were partly frozen with liquid nitrogen, and the well-stirred mixture was then placed around the tube containing the carbonyl selenide. The temperatures of the baths were checked by readings on a thermocouple. The results are shown in Table I, P being the vapour pressure (in cm. Hg) and T the absolute temperature. When log P was plotted against $1/T$ a straight line was obtained, and the b. p. found by extrapolation to be $-$ 22·8°/725 mm. This agrees well with the value of $-$ 22·9° obtained by Pearson and Robinson when they made a separate determination of the b. p. by a dynamic method at the above pressure. There can be little doubt that the previous high values were due to the presence of carbon

dioxide, as large amounts of this material were found by Pearson and Robinson in their crude preparation. From the slope of the line of the log P–$1/T$ curve the latent heat of vaporisation was calculated to be 49·3 cals. per g., a value that agrees well with that anticipated from Trouton's rule.

FIG. 1.

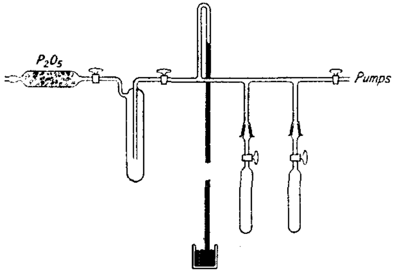


TABLE I.

Vapour Pressure of Carbonyl Selenide.

Bath.	Temp.	T.	P.	$\log_{10} P$.	$1000/T$.
$COMe_2$	−95°	178·0°	1·00	0·000	5·62
$CH_3{\cdot}CO_2Et$	−83·4	189·6	2·31	0·364	5·27
$CHCl_3$	−63·3	209·7	9·12	0·960	4·78
PhCl	−45·5	227·5	25·47	1·389	4·39
PhBr	−30·6	242·4	50·50	1·703	4·12
CCl_4	−22·9	250·1	72·29	1·859	4·00

(b) *The Decomposition of Carbonyl Selenide.*—When carbonyl selenide is passed through a heated tube, a sublimate of selenium is formed in the cooler portions of the tube, and conversely, carbonyl selenide is formed by the passage of carbon monoxide over heated selenium. Pearson and Robinson (*loc. cit.*) found that if the selenium was maintained at 500° the issuing gas contained 3·6% by volume of carbonyl selenide and at this temperature there is clearly an equilibrium $COSe \rightleftharpoons CO + Se$ with a concentration of carbonyl selenide somewhere near 3·6%. When the temperature is lowered, the equilibrium will be driven far over to the side of carbon monoxide and selenium, as the equilibrium constant will decrease and the concentration of the selenium vapour will fall off rapidly with temperature. Between our working temperatures of 120° and 140° the amount of carbonyl selenide formed cannot be detected, and one is concerned solely with its decomposition into carbon monoxide and selenium.

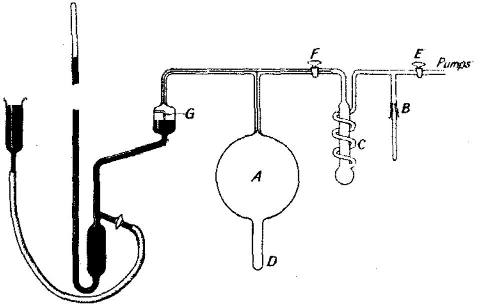
The apparatus used for following the decomposition is shown in Fig. 2. At the commencement of an experiment carbonyl selenide was transferred from the storage system to the reaction bulb A, through the standard ground-glass joint B, which at other times was closed by the taper as shown in the figure. After decomposition had proceeded for a given time, the contents of the bulb were slowly pumped off through the spiral C which was immersed in liquid nitrogen. This trapped the unchanged carbonyl selenide but allowed the carbon monoxide to be pumped away. Ten minutes' evacuation through a diffusion pump backed by a Hyvac pump sufficed to remove all the carbon monoxide, and, after the tap E had been closed, the carbonyl selenide could be condensed back into the tube D by cooling it with liquid air and allowing C to warm. Tap F was closed, and the pressure of the residual carbonyl selenide was measured by adjusting the reservoir so that the mercury level was just brought on to the small glass pointer G. The height between the mercury levels was then measured with the cathetometer. During the decomposition the mercury was pushed up to a fixed mark in the capillary tube so that all the carbonyl selenide was in the reaction bulb. This also served to keep clean the glass and mercury in the neighbourhood of the pointer so that later readings could be made without difficulty.

It is clear that the decomposition took place at a somewhat higher pressure than that measured, the true pressure, p, being 1·014 times the former when the room temperature was 20°.

The bulb *A* was surrounded by a heating bath of glycerol which had a gas thermoregulator and a stirrer bolted to the side so that the whole could be removed easily when the carbonyl selenide was being condensed back into the tube *D*.

The initial decomposition was on the clean glass bulb which had been baked out in vacuum. The glass was soon covered with an opaque film of selenium but the reaction was still very rapid. In 15 days it had fallen to one-hundredth of its initial value and thereafter there was no further systematic decrease, but a large fluctuation in the value of k about its mean value.

FIG. 2.



For a considerable time it was impossible to prevent or to discover the cause of these fluctuations, but it was obvious that the reaction was heterogeneous and extremely sensitive to slight changes in the surface. A clue was provided by the observation that after standing in vacuum at 130° over a week-end more decomposition took place on the surface than when it had only rested overnight, showing that the catalytic activity changed with time after the formation of the surface. To overcome these changes the reaction was allowed to proceed day and night, and was only interrupted for the short time required to pump off the carbon monoxide and to measure the decrease in pressure. The final pressure of one determination thus became the initial one of the next. Table II, in which p_0 is the initial pressure and t the time, shows that consistent results were obtained in this way. Determinations 1 and 2 are high, as no decomposition had taken place on the surface for the preceding 48 hours.

TABLE II.

Temperature 130°.

Detmtn. No.	p_0, cm.	t, mins.	$10^4\Delta p/\Delta t$.	$k \times 10^6$.	Max. error.	Detmtn. No.	p_0, cm.	t, mins.	$10^4\Delta p/\Delta t$.	$k \times 10^6$.	Max. error.
1	15·52	200	11	72	±8	6	13·62	1070	4·7	36	±2
2	15·30	1130	6·8	46	2	7	13·105	300	4·7	35	5
3	14·53	300	5·3	37	6	8	12·965	1080	4·5	35	2
4	14·37	1110	5·5	37	2		12·485				
5	13·76	300	4·7	35	6		(final press.)				

k (by summation of Nos. 3—8) = $(1/4160) \log_e 14{\cdot}53/12{\cdot}485 = 36{\cdot}5 \pm 0{\cdot}05 \times 10^{-6}$.

At this time the apparatus had to be left for 6 weeks, after which a further series of readings was made at 130°. Initially, $k = 376 \times 10^{-6}$, but the rate of decomposition decreased rapidly until after 6 days $k = 35 \times 10^{-6}$ and the series of results shown in Table III was then obtained. At pressures above 16 cm. the decomposition was unimolecular, but at lower pressures the constant k increased, showing that the reaction was proceeding more rapidly than expected. Determinations 4, 9, 14, and 19 were extended over 2 days in an attempt to obtain larger pressure changes and therefore greater accuracy. Unfortunately, the accumulation of the resulting carbon monoxide retarded the reaction and, as can be seen, the results were low. In subsequent work short runs were used, so the carbon monoxide could be pumped away before its effect

TABLE III.

	Temp. = 130°.			Temp. = 120°.		
Detmtn. No.	p_0, cm.	t, mins.	$k \times 10^6$.	p_0, cm.	t, mins.	$k \times 10^6$.
1	33·015	300	26	28·145	1110	27
2	*32·76*	*1080*	33	*27·315*	*300*	*26*
3	31·61	300	33	27·10	1070	28
4	31·295	2860	31·7	26·295	—	—
5	28·58	—	—	18·91	300	28
6	21·41	1100	31	18·745	1100	26
7	20·695	300	33	18·21	—	—
8	*20·49*	*1100*	*31*	13·565	*1080*	28
9	19·805	3000	29·5	13·165	300	31
10	18·13	—	—	13·045	1100	27
11	11·655	300	44	12·665	—	—
12	11·50	1060	45	7·96	1100	24
13	10·95	300	43	7·75	300	39
14	*10·81*	*2860*	*39·1*	7·66	*1160*	*26*
15	9·665	—	—	7·435	—	—
16	5·39	300	40	3·23	1080	25
17	5·325	1100	54	3·145	300	40
18	5·02	300	40	3·10	1100	28
19	4·96	3000	46·4	3·005	—	—
20	4·315	—	—	—	—	—

became appreciable. Further series of experiments were made at 120° and 140° and the results are given in Tables III and IV respectively.

TABLE IV.

Temperature 140°.

p_0, cm.	Final press., cm.	Mean press., cm.	t, mins.	$10^6\Delta p/\Delta t$.	$k \times 10^6$.	p_0, cm.	Final press., cm.	Mean press., cm.	t, mins.	$10^5\Delta p/\Delta t$.	$k \times 10^6$.
36·45	33·715	35·08	1120	244	69	15·54	15·08	15·34	300	153	100
25·85	33·15	34·50	1140	237	69	15·525	15·04	15·28	300	162	106
30·415	28·20	29·31	1100	201	69	13·42	11·90	12·66	1110	137	108
26·305	25·77	26·04	300	178	68	11·90	11·485	11·69	300	138	118
23·74	21·94	22·84	1125	161	70	7·485	7·205	7·345	300	93	127
19·04	*18·545*	*18·79*	*300*	*165*	*88*	*7·205*	*6·31*	*6·76*	*1090*	*82*	*121*
18·545	16·80	17·67	1100	159	90	2·975	2·86	2·92	300	38	131
17·61	17·12	17·36	300	163	93	2·86	2·515	2·69	1110	31	116

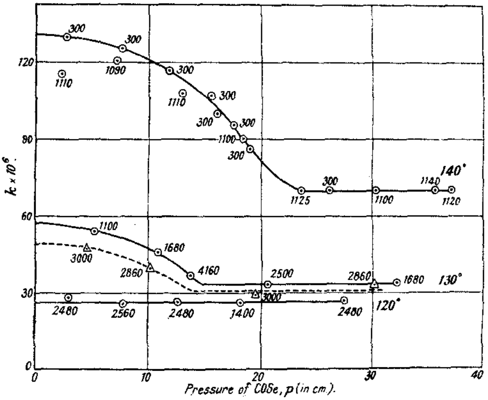
The results of all the determinations are collected together in the graph in Fig. 3, where the arithmetic means of the initial and final pressures of decomposition are plotted against the corresponding values of k calculated on the assumption that the unimolecular law was followed. It will be seen that at higher pressures k is constant at all three temperatures, but that at 130° and 140° it increases rapidly below certain critical pressures. The figures by the side of the points refer to the time in minutes of the decomposition, or summed decompositions, for which they are calculated. The lines are drawn preferentially through the higher points, which correspond with short periods of decomposition at 140°, where there has been little reaction and consequently only a small amount of the inhibiting carbon monoxide formed.

DISCUSSION.

It has been shown that the decomposition is extremely sensitive to changes in the selenium, which, except under special conditions, is not a constant catalytic surface. In view of the known allotropic complexity of selenium this is not surprising, as it might be expected that the element first deposited from the carbonyl selenide would go through one or more transformations before reaching inner equilibrium. This is supported by the deposition of red selenium observed when the carbonyl selenide is rapidly decomposed; *e.g.*, near the hot glass when a bulb containing the gas is sealed off. The red form slowly turns black and then appears identical with the black film observed in the decomposition bulb. It can therefore be postulated that the selenium is first deposited in a form indicated by Se-I and that this changes into a more stable variety, Se-II, at a rate depending on the temperature and on the quantity present. Hence, there can be two forms of selenium in the surface

and they have different catalytic activity towards carbonyl selenide, the form Se-II having the greater effect. For the higher pressures at 130° and 140° the amount of Se-I deposited by the carbonyl selenide is greater than that which changes into Se-II in the same time; hence the surface exposed to the gas is exclusively Se-I and the reaction is unimolecular. At a certain pressure the rate of change Se-I $\longrightarrow$ Se-II on the bulb equals the rate of decomposition COSe $\longrightarrow$ CO + Se, and Se-II can appear in the surface for the first time. This causes the unimolecular constant to begin to increase, but not $\Delta p/\Delta t$, which remains nearly constant for a time as more Se-II appears and the effect of its greater catalytic activity is manifest. It is clear that where decomposition proceeds on two surfaces a condition of equilibrium is set up, in which the amount of Se-I deposited equals the amount changing into Se-II in the same time, thus giving a constant surface at a given pressure. When

FIG. 3.



decomposition is arrested, the change Se-I $\longrightarrow$ Se-II can still go on, so the next decomposition is on a surface containing more Se-II and therefore gives the high value of k shown at the beginning of Table II. With intermittent working, the nature of the surface at the beginning of an experiment will depend on the extent of the previous decomposition and the time that has since elapsed, and consequently consistent results cannot be obtained.

If k_1 and k_2 are the velocity constants on the Se-I and the Se-II surface respectively, and if the rate of transformation of Se-I into Se-II is proportional to k_3 times the percentage of Se-I in the surface, it can be shown that the rate of decomposition $\Delta p/\Delta t$ is connected with the pressure p by the following relationship :

$$\Delta p/\Delta t = k_2 p/[1 + p(k_2 - k_1)/k_3] = k_2 p/(1 + K_2 p) \quad . \quad . \quad . \quad (1)$$

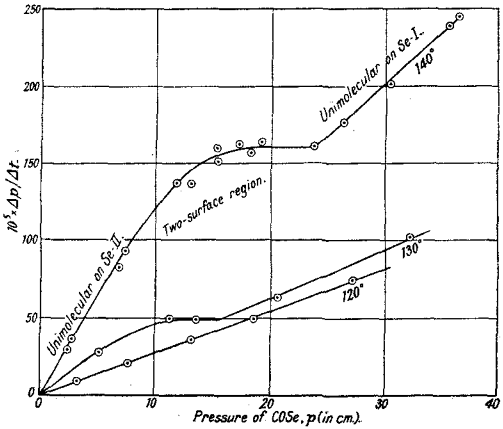
The second form of the expression is identical with Langmuir's well-known equation for a reaction with intermediate adsorption. A heterogeneous gas reaction, in which the catalytic adsorption was of the above type, would show a unimolecular reaction at low pressures and would tend to a zero-order reaction as the pressure increased. Similar effects are shown in the present case in the two-surface region as seen in Fig. 4, where the curve has a constant slope at low pressures and a horizontal portion at medium pressures, but the subsequent return to a unimolecular reaction on Se-I surfaces at still higher pressures shows that the results cannot be interpreted in terms of the Langmuir equation alone.

Values of k_2 and K_2 in equation (1) can be evaluated by the substitution of experimenta results: k_2 is the slope of the $\Delta p/\Delta t$—p curve when p approaches zero, and at 140° is equa to 125×10^{-6}; then, since $\Delta p/\Delta t = 161 \times 10^{-5}$ when $p = 23{\cdot}7$ cm., $K_2 = 0{\cdot}038$. Thes values of K_2 and k_2 enable $\Delta p/\Delta t$ to be calculated from, and plotted against, p. Th resulting curve, although of the right form, does not bend round so sharply as the experi mental one, and cannot be made to fit it. The deviation can be attributed to the condition for the transformation Se-I ⟶ Se-II being different from those postulated, the change fron 100% Se-I to 100% Se-II in the surface apparently occurring between the pressures 10—23·7 cm. It is possible to calculate the percentage y of Se-I in the surface from the equation

$$\Delta p/\Delta t = k_1 py + k_2 p(1 - y)$$

This has been done by taking $k_2 = 125 \times 10^{-6}$ and $k_1 = 69 \times 10^{-6}$, and when the resulting values of y are plotted against p the points, although rather scattered, appear to lie on a

FIG. 4.



straight line from 100% Se-II at 10 cm. to 100% Se-I at 23·7 cm. If this is so, the following modification of the formula enables $\Delta p/\Delta t$ to be accurately calculated from p in the two surface region:

$$\Delta p/\Delta t - 0{\cdot}00121 = 0{\cdot}000125(p - 10)/[1 + 0{\cdot}239(p - 10)]$$

Consequently, the decomposition at 140° may proceed according to three processes. Between $p = 0$ and $p = 10$ cm., and when p is greater than 23·7 cm., it is unimolecular on the Se-II and the Se-I surface respectively, whilst between 10 and 23·7 cm. it occurs on both surfaces simultaneously.

The allotropy of selenium is not sufficiently understood to enable a definite correlation with the above theory to be made. Nevertheless, the hypothesis is not out of harmony with the work of Briegleb (*Z. physikal. Chem.*, 1929, **144**, 321), who showed that the allotropy is to be attributed solely to dynamic equilibrium between the molecular species Se_8 and Se_1. The two forms called Se-I and Se-II above are probably the α- and the β-variety of monoclinic selenium, both being pseudo-equilibrium mixtures. These forms revert to the stable grey metallic form of the element, and it is this which appears ultimately in the reaction bulb. The very high value of k, 376×10^{-6}, obtained after 6 weeks' interval during which

no decomposition took place, is for the reaction on this surface. Consequently, the reaction velocity is much greater on the grey form than on the β-monoclinic variety, on which it is again greater than on the α-form. At the lowest pressure at which we have worked the grey selenium does not appear on the surface when decomposition is continuous; instead, the surface is Se-II (or Se_β) on which the unimolecular constant k_2 approaches a constant value that is larger than the corresponding constant for the Se-I (or Se_α) surface.

The carbon monoxide formed by the decomposition has an appreciable retarding effect at lower pressures as shown in Fig. 3, where the broken curve joins the values of k obtained when the carbon monoxide accumulates in the system. The effect is greater the lower the pressure, and at high pressures is small. This indicates that the carbon monoxide is strongly adsorbed on the Se-II only, where it displaces carbonyl selenide and reduces the decomposition rate. The effect of the carbon monoxide is greater at higher temperatures; at 140° it is measurable after 1000 minutes' decomposition at low pressures, whilst at 120° its influence cannot be detected.

The k–p curve at 120° does not show the characteristic break exhibited by the others, the reaction being unimolecular over the entire range examined. The values of k at zero pressure, by extrapolation from the curves in Fig. 3, are 27·5, 59·5, and 131, giving a temperature coefficient of 2·18 for each 10° rise. Therefore the surface at 120° over the *whole range* must be the same as that at zero pressure at 130° and 140°, *i.e.*, it is Se-II. The temperature coefficient enables a heat of activation to be calculated from the Arrhenius equation; its value is 24,600 cals./g.-mol.

The sudden break in the k–p curve takes place at a higher pressure at 140° than at 130°. This means that the rate of change of Se-I into Se-II is accelerated by this temperature increase to a greater extent than the decomposition of carbonyl selenide. The values of $\Delta p/\Delta t$ at these two points, *viz.*, 0·00161 and 0·00053 are measures of the rates of change of Se-I into Se-II, since in each case there is the same amount of Se-I, *viz.*, just sufficient to cover the surface completely. The temperature coefficient for the transformation Se-I $\longrightarrow$ Se-II is consequently 3·04.

Further work is in progress on the allotropic transformation of the selenium surfaces, which may establish that they are identical with the α- and β-modifications investigated by Briegleb. It is considered, however, that the kinetic data given prove the existence of dynamic allotropy in the surface, and that this constitutes the first investigated example of a gaseous decomposition which is dependent on a consecutive reaction in the catalytic surface.

SUMMARY.

The vapour pressure of carbonyl selenide has been redetermined and errors recorded in the literature corrected.

The decomposition of carbonyl selenide on selenium has been studied at 120°, 130°, and 140°. Two forms of selenium may be found on the surface which have been designated Se-I and Se-II. The decomposition is unimolecular on both allotropes but, under certain conditions, they may both be present together, and the reaction then appears complex. It can be interpreted in terms of the two unimolecular reactions and the percentages of Se-I and Se-II present in the surface.

ROYAL COLLEGE OF SCIENCE, LONDON, S.W. 7. [*Received, May 11th, 1937.*]

NOTES.

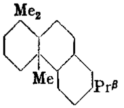
The Identity of α-Dihydrophyllocladene with Iosene. By LINDSAY H. BRIGGS.

IT has been shown previously that the lignite hydrocarbons, iosene, bombiccite, branchite, hofmannite and the hydrocarbon from Terni lignite are identical (Ciusa and Galazzi, *Gazzetta*, 1921, **51**, i, 55; Ciusa and Croce, *ibid.*, 1922, **52**, i, 125; Soltys, *Monatsh.*, 1929, **53—54**, 175).

Professor Ciusa has kindly forwarded samples of bombiccite and the hydrocarbon from Terni lignite. These do not depress the melting point of the diterpene derivative, α-dihydrophyllocladene (identical with dihydrodacrene and dihydrosciadoptiene; Briggs, this vol.

p. 830), so the latter also is identical with iosene (the name iosene is preferred to the prior synonyms). The rotation, $[\alpha]_D^{22^\circ}$ + 23·25° (c = 1·118 in absolute alcohol) (Nishida and Uoda, *J. Agric. Chem. Soc. Japan*, 1936, **12**, 308, give $[\alpha]_D^{20^\circ}$ + 22·8° in chloroform), also agrees with that recorded for iosene by Soltys, $[\alpha]_D^{22^\circ}$ + 23·75° (absolute alcohol). This observation is of interest to palæobotany as a link between living and fossil plant products.

On the basis of selenium dehydrogenation of iosene to retene, Soltys (*loc. cit.*) has proposed alternative formulæ for iosene. Although no conclusive evidence is yet available, the annexed formula for the carbon skeleton of iosene is equally compatible with the evidence of dehydrogenation, it conforms with the isoprene rule, and has the advantage of falling into line with the structures of abietic acid and fichtelite (Ruzicka and Waldman, *Helv. Chim. Acta*, 1935, **18**, 611). The position and nature of the fourth ring are unknown, but Soltys's suggestion that it is 3-membered does not harmonise with the absence of reactivity towards bromine.—AUCKLAND UNIVERSITY COLLEGE, AUCKLAND, NEW ZEALAND.



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The Spontaneous Polymerisation of Liquid Propaldehyde. By ERNEST J. BUCKLER.

IT does not seem to have been recorded hitherto that pure liquid propaldehyde is an unstable substance, liable to sporadic polymerisation. In the course of work on this substance, specimens either were taken from B.D.H. samples or were obtained by the oxidation of propyl alcohol with chromic acid. Their stability was not improved by rigorous drying, or careful fractional distillation in air, or evaporative distillation in a vacuum; in fact, intensive purification seemed rather to favour polymerisation. It seemed immaterial whether the substance was stored in Pyrex or in soda-glass, in air, inert gas, or a vacuum, in the light or in the dark, but polymerisation occurred more readily the lower the temperature at which it was stored.

The mobile aldehyde first became viscous, and insoluble in water; its vapour pressure at 0° fell from 105 mm. to 10 mm. Hg, and its aldehydic properties became less pronounced. The product had no definite boiling point, and its molecular weight in benzene, as found by the cryoscopic method, indicated that the mean number of propaldehyde units per molecule was 2·8.

In the next stage, which may occur spontaneously at room temperature, or more rapidly on heating, the liquid darkens, and divides into two layers, the lower one of which was found to be water, containing a little unchanged aldehyde. This suggests that an aldol condensation had occurred, followed by elimination of water.

The upper layer was submitted to evaporative distillation in a vacuum, until a dark brown, involatile, viscous liquid remained, whose empirical formula corresponded to that of methylethylacraldehyde (Found : C, 73·2; H, 11·1. Calc. for $C_6H_{10}O$: C, 73·5; H, 10·2%). It had no definite boiling point, and no aldehydic properties, and its molecular weight in benzene was 265, which implied a mean association of 2·7 methylethylacraldehyde units. Its empirical formula, molecular weight, and chemical properties were not altered by heating at 120° in a vacuum for 48 hours (Found : C, 73·6; H, 11·1%).

The volatile portion of the upper layer was a colourless liquid, with no definite boiling point, and no aldehydic properties, and had an empirical formula corresponding most closely to that of propaldehyde (Found : C, 63·4; H, 10·3. Calc. for C_3H_6O : C, 62·1; H, 10·3%). Its molecular weight in benzene increased as the solution became more concentrated, and indicated a mean association of 2·8 propaldehyde units. This polymer seemed to be of the aldol type, since when it was heated for a short time in a vacuum at 120°, water separated, and the residue had the same composition and properties as the involatile oil previously described. Neither commercial firms, nor ourselves, have found any effective stabiliser for the aldehyde.

The author's thanks are due to the Chemical Society, and the Department of Scientific and Industrial Research for grants, and to Prof. R. G. W. Norrish, F.R.S., for helpful advice and criticism.—THE DEPARTMENT OF PHYSICAL CHEMISTRY, CAMBRIDGE. [*Received, May 13th*, 1937.]

The Alkaloid of Solanum Auriculatum, *Ait.* By A. R. ANDERSON and LINDSAY H. BRIGGS.

GRESHOFF (*Ber.*, 1890, **23**, 3541; *Ber. Deut. pharm. Ges.*, 1899, **9**, 214) found that *Solanum auriculatum* Ait. is rich in " solanine," and a gluco-alkaloid sintering at 256° and slowly decomposing above 272° has now been obtained from the unripe berries by the method used by Oddo

(*Gazzetta*, **1911**, **41**, i, 490) for the isolation of solanine-s from *S. sodomeum*. This alkaloid did not depress the decomposition point of solanine-s; with which it may be identical, since it gave the same colour reactions with alcoholic sulphuric acid. The aglucone, obtained by hydrolysis with alcoholic hydrogen chloride, separated from alcohol in needles, m. p. 216—219°, which raised the m. p. (197·5—199·5°) of authentic solanidine-s to 212·5—216·5° but depressed that of solanidine-t by 20°. It is probably an isomorphous form of solanidine-s, since it gave the same colour reactions and afforded derivatives melting at the same temperatures as those obtained from the lower-melting specimen, and no depression in m. p. was observed on admixture of the respective pairs. The following derivatives were prepared from both specimens and the melting points recorded by Oddo (*loc. cit.*) are given in parentheses: Hydrochloride, 309·5° decomp. (302—303° decomp.); hydrobromide, 283° decomp. (283—284° decomp.); picrate, 141·5—142° (decomp.), after sintering at 136° (144—145°); *o*-nitrobenzoate, 219° decomp. (222°).

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The Polymorphism of Chalkone. By R. J. W. LE FÈVRE.

DURING the preparation of chalkone for work already described (J., 1933, 344), it was noticed that the m. p. of apparently pure specimens of chalkone could be materially altered by a single fusion. Later, following Weygand and his collaborators (*Ber.*, 1929, **62**, 2603, and other papers), a sample with m. p. *ca.* 30° was obtained by seeding a melt with a minute crystal of dibenzoylmethane, and its polarisation in benzene solutions compared at 25° with that of the normal form, m. p. *ca.* 58°. The incidental measurements are recorded below; f_1, ε, and $d_{4^\circ}^{25^\circ}$ refer respectively to the molar fractions of the solute in the solutions, to the dielectric constants, and to the densities. Since the last two properties are linear with f_1, the expressions $\varepsilon = \varepsilon_2(1 + \alpha f_1)$ and $d = d_2(1 + \beta f_1)$ are applicable.

	f_1.	ε.	$d_{4^\circ}^{25^\circ}$.	$\alpha\varepsilon_2$.	βd_2.
Benzene	0	2·2725	0·87380	—	—
Chalkone, m. p. 58—59°	0·01201	2·4385	0·87968	13·819	0·4895
	0·01751	2·5128	0·88230	13·722	0·4854
	0·02205	2·5751	0·88451	13·723	0·4867
	0·02811	2·6589	0·88749	13·746	0·4870
Chalkone, m. p. *ca.* 30°	0·01501	2·4801	0·88101	13·831	0·4803
	0·02261	2·5806	0·88476	13·627	0·4847
	0·02565	2·6255	0·88636	13·762	0·4897
	0·02959	2·6799	0·88830	13·768	0·4900

The essential constancy of $\alpha\varepsilon_2$ and βd_2 for the two solutes suggests that they are polymorphs and not geometrical isomerides. These results thus confirm those recently published by Eisenlohr and Metzner (*Z. physikal. Chem.*, 1937, **178**, *A*, 350) relating to chalkone modifications of m. p. 49°, 57°, and 59°, for which moments 3·02, 2·98, and 3·00 D respectively were reported.

Calculated from the equation ${}^\infty P_1 = A(M_1 - B\beta d_2) + C\alpha\varepsilon_2$ (cf. J., 1936, 491) with the data tabulated above (mean $\alpha\varepsilon_2 = 13{\cdot}750$, mean $\beta d_2 = 0{\cdot}4865$), ${}^\infty P_1 = 257{\cdot}8_8$ c.c. (for the benzene used, $A = 0{\cdot}34085$, $B = 89{\cdot}265$, $C = 14{\cdot}670$). Auwers and Eisenlohr (*J. pr. Chem.*, 1911, **84**, 67) found $n_D^{62\cdot3^\circ}$ 1·6458 and $d_{4^\circ}^{62\cdot4^\circ}$ 1·0712, whence $[R_L]_D = 70{\cdot}5$. The present measurements, therefore, correspond to a moment of $3{\cdot}0_1$D units; the good agreement with Eisenlohr and Metzner's result suggests that Bergmann's value for chalkone (2·92 D) (J., 1936, 402) is somewhat low.—UNIVERISTY COLLEGE, LONDON. [*Received, May 13th*, 1937.]